SEIFERT AND MUELLER

PHYSICAL AND CLINICAL DIAGNOSIS

E. COWLES ANDRUS, M.D.

25/-

Diagnosis

MANUAL OF PHYSICAL AND CLINICAL DIAGNOSIS

BY

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PREFACE TO THE FIRST EDITION

WE WERE prompted to prepare this manual by our revered teacher and chief, Geheimrat Professor C. Gerhardt.

It is intended to meet the demand for a succinct presentation of the methods of examination and to furnish a collection of those data, a knowledge of which is an ever-present necessity to the physician at the bedside. On the one hand these data, on account of their quantity and diversity, can only with difficulty be accurately memorized; on the other hand they are distributed in so many text-books and monographs that it is toilsome and time-consuming to hunt them out upon each occasion.

In the selection and arrangement of material we have been guided by the experience of teaching. We have endeavored to take into consideration the practical requirements of clinical examiners and physicians, to include only pertinent information and to omit the non-essential and obvious.

THE AUTHORS

INTRODUCTORY PREFACE

A WORK on diagnostic methods by the master and great clinical teacher, Friedrich Mueller, needs no recommendation from anyone. The twenty-four editions in the German language and the numerous editions in seven other languages attest to the value of this compendium of diagnostic methods and data. American medical students, internes and practitioners should feel very grateful to Dr. Andrus for translating this outstanding work. As a teacher of internal medicine, I am delighted that this work is now available to our students and internes. Every interne and clinical clerk should carry a copy in his white coat to be available when working on the wards or in the clinical laboratory. The student who has had a course of lectures on physical diagnosis and on clinical microscopy and chemistry will find that this little book is all that he will usually need to consult in his work on the wards. The practitioner of medicine who has a copy on his desk will only rarely have to consult any other work on diagnostic methods and data.

GEORGE E. FAHR

University of Minnesota

TRANSLATOR'S PREFACE TO THE SECOND EDITION IN ENGLISH

The purpose and scope of such a book as this are expressed by the authors in their preface to the first edition. The requirements of the physician and student at the bedside are by no means bounded by a single language. To fulfil these needs in English this translation has been undertaken from the latest, the thirty-first, edition.

Certain additions have been made to include procedures to which the American student and physician are accustomed: blood chemistry, staining methods, etc. All temperature charts have been furnished with the Fahrenheit scale in addition to the Centigrade of the German edition.

It is a pleasure to express my appreciation to Dr. G. E. Fahr, University of Minnesota Medical School, as representative of the author, for permission to translate this work and for many helpful suggestions. I desire also to acknowledge the aid of fellow-members of the Department of Medicine, Johns Hopkins University—Drs. Perrin H. Long and Maxwell M. Wintrobe who have reviewed the chapters on Infectious Diseases and Blood. I wish finally to record my thanks to Rebecca S. Marshall for her assistance in preparing the manuscript of the present edition.

The Translator

Johns Hopkins University

TABLE OF CONTENTS

CHAPTER XI

MANUAL OF PHYSICAL AND CLINICAL DIAGNOSIS

CHAPTER I

INTRODUCTION

The clinical record consists of three portions; first **anamnesis,** second the **status præsens** or physical examination, and third the no less important **supplementary information** concerning the general course of the disease as well as the nature and the result of treatment.

ANAMNESIS

Its object is to provide a complete and sequential record of the patient's illness; it should constitute a background against which to view his physical condition at the time of examination. As such it should include all pertinent details concerning family, home and environment, the previous state of health of the individual, and the development of the condition which brings him to the physician. The anamnesis is obviously different for each patient; its value is often determined by the degree to which it distinguishes the case at hand from other, perhaps similar, cases. No universally applicable scheme can be laid down; experience and tact are required, in addition to a comprehensive knowledge of disease, so to question the patient that a correct and complete picture may be obtained. The following outline may, however, serve as a guide.

Chief complaint and its duration.[1]

Family History.

State of health or cause of death of parents, brothers, or sisters, with ages at death. History of tuberculosis (giving

[1] Throughout the history actual **dates** should be recorded, not simply the day of the week.

patient's association therewith), rheumatism, gout, nephritis, heart trouble, diabetes, cancer, nervousness or insanity, goiter, hæmophilia, obesity, arteriosclerosis or hypertension.

If there be an hereditary disease in the family, such as hæmophilia, inquire into the condition of the grandparents, aunts, uncles and cousins.

Past History.

General health and robustness (ever rejected for life insurance, army, etc. If so, state cause).

Acute infectious diseases—measles, mumps, whooping-cough, chicken-pox, typhoid, pneumonia, pleurisy, scarlet fever, diphtheria, acute rheumatic fever, chorea, malaria, tonsillitis.

If other infections are mentioned, specific statements must be made concerning them; the history of any acute infection should include a record of its duration, severity and complications.

Operations or injuries.

Head.

Headaches, trauma.

Eyes—vision, diplopia, inflammatory disease.

Nose—colds, obstruction, epistaxis.

Ears—hearing, earache, discharge, tinnitus.

Teeth—pain, bleeding or receding gums.

Throat—sore throats, tonsillitis, hoarseness, sore mouth or tongue.

Respiratory—pain in chest, dyspnœa, cough, sputum, hæmoptysis, night-sweats.

Cardiac—pain or distress over præcordium, radiation of pain, palpitation, dyspnœa, orthopnœa, œdema, cyanosis.

Gastro-Intestinal—habits of eating, appetite and digestion, pain and its relation to eating, eructation, nausea and vomiting, hæmatemesis, regularity of bowels, catharsis, diarrhœa, stools (clay-colored, tarry, fresh blood), hæmorrhoids, jaundice.

Genito-Urinary—dysuria, pain, nocturia, hæmaturia, polyuria, oliguria, retention, incontinence, œdema.

Gonorrhœa, syphilis (primary and secondary) (inquire

by name and symptoms), soft chancre, bubo, glands, mucous patches.

Menses—onset, regularity, dysmenorrhœa, menorrhagia, last period, leucorrhœa.

Neuro-Muscular—nervousness, insomnia, vertigo, fainting, tremors, convulsions, paralysis, paræsthesia, memory, disposition, drowsiness, fatiguability, neuralgic or lightning pains, deformity or disability of joints, muscular pains, lameness or weakness.

Habits, environmental influences and personal history.

Marital—duration; health of partner; children, giving age and health; miscarriages chronologically, giving duration of pregnancy in each.

Habits—regularity of eating and sleeping; exercise; tea, coffee, tobacco, alcohol, drugs, or medicines.

Occupation—past and present work; conditions of work; hours of work, day or night; physical or mental strain; exposure to cold, heat, dust, etc.; type of work, ventilation, overcrowding, etc.; possible exposure to metals, particularly lead, arsenic, chromium, or to possible poisonous gases.

Home conditions—presence of epidemics; diseases such as malaria or hook-worm prevalent in district. In certain cases inquire about water and milk supply and other possible sources of infection; exposure to communicable disease; residence in tropics.

Weight—average weight, best weight, with date; present weight; and duration of recent loss or gain.

Present Illness.

Describe as accurately as possible the course of the present illness. If there is gradual transition from a past state of ill health to the present illness, make this quite clear. There can be no outline for the present illness which would be applicable to all cases. No matter what the disease, the story can be told in a logical sequence. The onset of the illness should be carefully dated. If the onset is acute the state of health immediately prior to this should be determined and a careful description given of the earliest symptoms of onset. In the acute infections or intoxications inquiry should be made concerning a pos-

sible incubation period and such symptoms at the onset as chills, fever, headache, gastro-intestinal disturbances, cough, regional pain or any other general or local symptoms. When the present illness has progressed in attacks separated by free intervals, it is necessary to obtain the history of a typical attack—onset, duration and associated symptoms such as pain, chills, fever, jaundice, hæmaturia, etc. Inquiries should be made as to whether these attacks were related to any activity of the patient, or to such factors as diet, excitement, etc. In both acute and chronic illnesses the date at which the patient stopped work or went to bed should be noted, and inquiry made as to whether the patient thought that he was improving or becoming worse. The course of the disease should be developed symptomatically in chronological order, each symptom thoroughly developed in its course up to the patient's admission to the hospital. When there is a conspicuous disturbance of a particular organ or system, direct questions should be asked as to all possible symptoms referable to the disturbance of this system. Inquiry should finally be made as to any abnormalities referable to all systems (as in Past History above) and a note made as to whether or not there has been pain, cough, dyspnœa, nausea, vomiting, etc. Patient's previous treatment should be noted identifying if possible medication received.

At the end of the history a note should be made as to whether the history was obtained from the patient, relative, friend or physician, the mental condition of the patient and the probable reliability of the history.

Although the anamnesis is recorded in the order: complaint, family history, past history, present illness, it is preferable, in interviewing the patient, to proceed in the following order: complaint, present illness, past history, family history.

STATUS PRÆSENS

The physical examination should be recorded precisely and yet as completely as possible. Its record should follow the various organ-systems. The following outline is suggested:

General. Height, weight, build (stocky or frail).

Skeletal system.

State of nutrition. Musculature, subcutaneous fat.

Condition of the skin. Ruddy or pale, abnormally flushed, cyanotic, icteric, bronzed, œdematous; cutaneous eruptions, scars, decubitus ulcers.

Strength, position, posture.

Mental status. Intelligence, consciousness (whether sensorium is clear or beclouded), restlessness, jactitation, delirium, apathy, stupor, sopor = drowsiness, coma = loss of consciousness with abolition of reflexes. Speech (aphasia, anarthria, dysarthria, stuttering, pararthria syllabaris = confusion of syllables and letters), memory, vertigo.

Body temperature.

Head. Contour of skull. Distribution and abnormalities of the hair. Facial expression and musculature (are both sides of the face equally movable?). Lid-slits equal? Ask patient to wrinkle the forehead, close the eyes, purse the lips and show the teeth, whistle, inflate the cheeks.

Eyes. Position, movements, pupils (shape, size, equality, reaction to light with convergence or accommodation), sight, color-vision, range of accommodation, conjunctivæ, ophthalmoscopic examination.

Ears. Hearing, tenderness over the pinna or mastoid process, otoscopic examination.

Nose. Shape, secretion, sense of smell, patency of air passages, naso-pharyngoscopic examination.

Lips. Pallor, dryness, crusty or greasy covering, rhagades, herpes.

Teeth, Gums. Oral mucous membranes, salivary secretion.

Tongue.—Is it protruded directly (in the midline) or obliquely, with or without tremor; unilaterally atrophic? Fibrillary twitchings? Is its mucous membrane pale or red, moist or dry; is the surface of the tongue abnormally smooth as a result of papillary atrophy (e.g. in pernicious anæmia or late syphilis) or furrowed from hypertrophy of the papillæ? Is the tongue coated? Is the coating white

in color, or of a brown greasy consistency? Leukoplakia? Palate, pharyngeal mucous membrane, tonsils (defects or scars, ulcers, color, swellings, deposits, concretions). Is the palate abnormally high? Ability to swallow, taste.

Neck. Length and circumference; thyroid; lymph glands, in particular those at the angle of the jaw which drain the throat; and the cervical glands, which are often palpable in syphilis and tuberculosis as well as in cases with inflammation of the scalp. Leukoderma (a sign of secondary syphilis). Scarred glands (tuberculosis).

Pulsations of the carotid arteries and jugular veins.

Larynx and voice. Laryngoscopic examination. Cough. Œsophagus, impediment to deglutition, examination with œsophageal sounds and X-ray.

Condition of the spine (straight or curved, mobile or stiff). Gibbus, tenderness on percussion or pressure upon the head.

Thorax. Form and elasticity of the thoracic cage. Circumference of chest at end of inspiration and expiration. Is there any deformity of chest or ribs? Supra- and infraclavicular fossæ. Are both halves of the thorax symmetrical or is one side retracted or protruded? The affected side is to be distinguished by the fact that its respiratory movements are comparatively diminished. Type of breathing. Respiratory rate. Tactile Fremitus.

Lungs. Percussion of the lungs, comparison of the lung apices, determination of the position and respiratory excursions of the lung borders.

Auscultation of the lungs, breath sounds, râles, friction rubs, voice sounds, **vocal fremitus.**

Heart. Position and characteristics of the cardiac impulse, palpable or visible pulsations over præcordium, epigastric pulsation. Abnormal pulsations elsewhere in the chest, particularly in the first and second intercostal spaces (aneurysm of the aorta). X-ray examination.

Percussion of the cardiac dulness (relative and absolute dulness).

Auscultation of the heart.

Blood vessels. Condition of the systemic arteries, rigidity, tortuosity.

Radial pulse and veins, filling and pulsation. Blood pressure determination. Electrocardiography.

Abdomen. Circumference, distension, percussion and palpation. Tumors, fluctuation, areas of tenderness. Ascites. Umbilicus.

Examination of **liver** and **spleen** by palpation and percussion. Friction fremitus (auscultation).

Size of **stomach**, after inflation, succussion, tumors, tenderness to pressure. Removal and examination of gastric contents when indicated. X-ray examination.

Examination of **anus** and **rectum**. Digital and proctoscopic examination. Condition of inguinal rings. Herniæ.

Percussion and palpation of the **kidneys,** Function of **bladder.** (Passage of urine, retention, percussion and palpation of the bladder.)

Examination of **genital organs:** In the male, scars on penis, condition of testes and epididymi, prostate, inguinal glands.

In the female, pelvic examination when indicated.

Are the genital organs and the secondary sexual characteristics (voice, beard, axillary and pubic hair, breasts, pelvis) normally developed, imperfectly developed (hypogenitalism, infantile habitus), over-developed (hypergenitalism), or abnormal?

Extremities. Position and posture of the limbs, condition of the bones, joints, and musculature. (Atrophy, hypertrophy, tonus and strength of the muscles.) Are the extremities straight or are bow-legs or knock-knees present, (Genu varum or valgum). Flat-foot (does the medial portion of the sole of the foot touch the floor on standing), or incomplete flat-foot. Are the shins sharp or thickened (the latter in syphilis). Venous varicosities. Scars of leg ulcers.

Hand: Condition of joints and fingers. Trophic changes in skin or nails.

Mobility. Abnormal, involuntary movements, tremors, athetosis, chorea; voluntary movements, resistance to passive motion, strength of muscles, ataxia, ability to perform complicated movements (finger-to-finger, finger-to-nose), grip, writing, gait, stance, Romberg.

Sensitivity of skin for touch, pain, heat, cold, and pressure. Muscle sense vibratory sense. Pressure over nerves.
Reflexes. Skin and tendon reflexes.
Examination of urine (amount, color, specific gravity, albumin, sugar, etc.), and urinary sediment (microscopic examination).
Examination of sputum (macroscopic description and microscopic examination). **Amount and characteristics.**
Examination of gastric contents or vomitus.
Examination of fæces.
Examination of blood.
Finally an outline of the therapy prescribed (medication, diet, baths or other therapeutic procedures).

SUPPLEMENTARY RECORD

This should include, among other data, all further observations and the results of examinations made upon the case at hand. The body temperature, pulse rate and respiratory rate are best presented in the form of curves. A continuous record of the body weight is particularly indicated in chronic cases in order to follow the progress of the disease. Therapeutic measures as well as their results should also be recorded.

By **morbidity** one understands the relation of the number of patients to the total living population, by **mortality** the number of those dying to the total population and by **fatality** the proportion of those dying to those sick.

CONSTITUTION AND HEREDITY

The origin and course of diseases depend not only upon environmental influences, such as trauma and infection, but also upon the characteristics of the individual, and especially upon his powers of resistance. These properties are collectively denoted as the **constitution,** a term which includes all the bodily and mental attributes which any individual possesses at a given time. The constitution of a person can only be approximately classified according to conformation. One can, indeed, distinguish a small compact (**pyknik**) body frame, a long thin (**asthenic**) type which is often characterized by muscular under development, low blood pressure and fatiguability, and an intermediate, **ath-**

letic or hypoplastic type. However, such differentiation is not entirely satisfactory, and its relation to the incidence of disease is not entirely clear.

The individual constitution is inevitably influenced by environmental factors: (education, good or bad nutrition, diseases, acquired immunity or allergy, occupational hazards, etc.). Most important, however, are those characteristics which the individual has received through inheritance from his ancestors. The inherited characteristics of an individual are designated as the **idiotype,** in contrast with the **phanutype,** a term which describes the individual both as to inherited (idiokinetic) and acquired (parakinetic) characteristics.

At the time of fertilization the nucleus of the ovum is united with that of the spermatozoön in such a way that the new-formed primary cell (zygote) receives exactly the same amounts of nuclear substance, and with it the chromosomes, from both father and mother. Likewise, with each subsequent division of the fertilized ovum, each cell of the embryo and of the developing individual receives equally the inheritances and tendencies of both the paternal and maternal organisms. But, as all the cells of an individual organism have resulted from the sexual union of preceeding parental generations, the fertilized egg receives not only the inheritances of both parents but also those of the grandparents, etc.

If the paternal and maternal organisms possess the same characteristics in every respect (homozygote) their offspring will resemble each other completely, except as in later life environmental influences or disease (parakinetic factors) may produce somatic changes. A complete homogeneity of inheritances from the paternal and maternal organism (pure inheritance) may occur in pure-bred plants and animals but never in human beings. If the paternal and maternal organisms offer real differences in their inheritances (idioplasm), they are **heterozygotes.** Their offspring will be hybrid and will possess characteristics received from both the paternal and maternal organisms.

The laws, according to which the qualities of an heterozygous set of parents affect the first and subsequent genera-

tions of descendants, were discovered by Gregor Mendel in 1865 in a study of variegated plants. The Mendelian laws of inheritance have been proved to apply not only to plants but also to animals, and to man as well.

For example, if the ovum of a red-blooming Four-o'clock flower be dusted with the pollen of the white-blooming variety, the first generation (F 1) shows the mixed characteristics of both parents: the flowers are neither white nor red but rose-colored. However, if this first rose-colored generation be intercrossed the result is that in the second generation (F 2) half of the plants produce rose-colored blossoms, one fourth pure red and one fourth pure white. The red-blooming members of the second generation produce when interbred only a pure red, and the white variety only a pure white generation, while the rose-colored plants divide again according to the above-mentioned rule and produce one-fourth red, two-fourths rose, and one-fourth white, offspring. Mendel's law postulates that the inherited characteristics in each gamete are implanted double (paired) and that they are divided into two equal halves by transmission.

These laws of inheritance apply only in case the distinct characteristics of differently pre-disposed individuals (e.g., the red and white blossoms) are transmitted equally. But if the hereditary characteristics of one of the pair preponderate, i.e., if these are "dominant," the first generation will show only the characteristics of the dominant parent. Thus, the first generation, through dominance of the red blossoms includes only red-blooming examples which outwardly are not different from red-blooming parents. But the fact that, in these red-blooming examples, the inheritance from the white-blooming parent is still present though "recessive" is shown by the result that, in the second generation, though three-fourths of all the plants produce red, one-fourth produce white blossoms, and that, in succeeding generations, a few white-blooming plants continue to appear.

Such dominant hereditary characteristics are of great significance in human beings, both to the advantage and disadvantage of the individual. They tend to become manifest in the first generation. As examples may be mentioned the thick lower lip of the House of Hapsburg, hereditary

(Huntington's) chorea, congenital myotonia, night-blindness, haemolytic icterus, hypertension and, in certain families, diabetes.

On the other hand, if an hereditary characteristic is **recessive** it does not appear in the first generation and may not do so later. However, its tendency can be transmitted through further generations and may appear occasionally. This is the case if an individual affected with such a recessive characteristic produces a child by a partner from a family which offers this same latent hereditary trait. This phenomenon is most frequently manifested in case of **consanguinity** between the parents. To these recessive hereditary diseases belong certain forms of deaf-mutism, albinism, Friedreich's disease (familial spinocerebellar ataxia), alkaptonuria, xeroderma pigmentosum, and finally also certain mental diseases such as dementia præcox. Many endogenous diseases appear in some families as dominant and in others as recessive hereditary characteristics, e.g., muscular dystrophy, lenticular cataract and otosclerosis. In bronchial asthma, epilepsy, migraine and goiter the hereditary type is not fixed.

Many hereditary diseases characteristically occur only in one sex, either in the male or the female descendants. To these "sex-linked" hereditary diseases belong color-blindness and certain blood diseases (e.g., hæmophilia). These almost always affect only the male members of the family, although the female individuals exhibit their latent predisposition in the fact that their sons are subject to this disease. Pernicious hereditary factors may either be evident at birth as deformities (e.g., too many or too few fingers) or may first become manifest in later life and then lead to progressive disease (e.g. muscular dystrophy).

There is, in the usual sense of the word, no "Inheritance of acquired characteristics." However, the circumstances of the environment and, therewith, vital conditions, may affect the germ plasm and thereby, while not altering the individual himself, affect his descendants and result in hereditary changes of the idiotype which may pass on to succeeding generations. This process is denoted as idiokinesis, variation or mutation. The phylogenetic history of plants,

of animals and of man indicates that in the course of time idiokinesis has wrought many changes among the races.

BODY TEMPERATURE

The body temperature may be measured in the axilla with sufficient accuracy to determine whether or not a fever exists. If, however, it is necessary to determine slight deviations from the normal, e.g. in suspected tuberculosis, the measurement is best carried out per rectum or in the mouth with the thermometer beneath the tongue and the lips closed. Such measurements are only accurate if taken while the patient is at rest. It is, moreover, useless to attempt an exact determination of body temperature within a half-hour after a meal or following violent exercise. (In tuberculosis, during the convalescence from a severe illness, or in weakened or nervous individuals the mechanism of heat regulation is sometimes abnormally labile. As a result exercise of a not unusual degree, such as a walk, or mental excitement or a mild disturbance of digestion may produce a transient rise in temperature.) Such an elevation is of no particular diagnostic significance.

The thermometer must remain in place for at least five minutes. In the rectum the temperature tends to be approximately a half-degree higher than in the mouth; however this difference is often less and sometimes, particularly in febrile conditions, may be still greater, that is a whole degree or more.

The temperature of a healthy individual as measured under the tongue or per rectum is from 36.0 to 37.2° centigrade.[1] It varies in health by only a few tenths of a degree in the course of a day. The maximum is reached in the afternoon and the minimum in the early hours of the morning. Variations of temperature of an entire degree or more in the course of the day cannot be regarded as normal. The converse, on the other hand, is also to be regarded as abnormal, i.e. if the morning temperature is higher than that in the evening. This

[1] In comparing the various thermometric units the following formula is employed:

n° Centigrade = 4/5 n° Reamur = 9/5 n° plus 32° Fahrenheit.

36° C	= 96.8° F	38° C	= 100.4° F	39.5° C	= 103.1° F
37°	= 98.6°	38.5°	= 101.3°	40°	= 104.0°
37.5°	= 99.5°	39°	= 102.2°	41°	= 105.8°

typus inversus, as well as increased daily variations of temperature, occur in tuberculosis and certain other conditions.

Transient elevation of temperature may occur also in healthy individuals and particularly in hot or steam baths in which loss of heat from the body surface is suppressed. The prevention of heat-loss may result in a high, and in itself, dangerous, temperature elevation (heat stroke) as, for example, when violent exercise is undertaken in hot, sultry weather. Here the increased heat resulting from the work involved cannot, as result of diminished production or insufficient evaporation of perspiration, be given up from the body surface. If, on the other hand, it is possible by means of removal or evaporation of the sweat for the normal discharge of heat from the body surface to take place even extreme exertion produces no elevation of temperature in normal individuals.

High and persistent elevations of temperature occur principally in fever and most frequently as a result of infection. The degree of temperature elevation is no adequate measure of the severity of an illness. Rise in body temperature may also occur in the absence of infection, as, for example, in the absorption of hæmorrhage or of the secretion of a wound (post-hemorrhagic and absorption fever, e.g. after a fracture or in the case of the accumulation of blood and secretion in the puerperal uterus), also in blood diseases (severe anæmia, hæmoglobinæmia and hæmoglobinuria), in leukæmia, and in hyperthyroidism. In hysterical individuals an apparent rise in temperature without further manifestations of disease suggests that this may have been accomplished artificially by friction upon the thermometer.

In fever also the body temperature shows a diurnal variation, indeed often greater than that encountered in the normal. The difference between the highest and the lowest temperature observed in a single day determines the type of fever:

Febris continua = Daily variation of not more than 1°.

Febris remittens = Daily variation of not more than 1.5°.

Febris intermittens = The alternation during the day of febrile and afebrile intervals.

In the course of a febrile illness the following stages are distinguished:

Stadium incrementi = rise in temperature. More rapid rise in temperature follows a chill. As a result of the contraction of the superficial vessels of the skin the heat loss from the surface of the body is diminished; there is an accumulation of heat and a consequent rise in body temperature. In conditions characterized by a gradual rise in temperature, e.g. typhus fever, chills are slight or wanting.

Fastigium = stage of high fever.

Stadium decrementi, defervescence may take place gradually over a period of several days: fall by lysis, or suddenly: crisis. In a true crisis the temperature falls rapidly (within one day) to normal or less. Occasionally it is preceded by a considerable though transient elevation of temperature = perturbatio critica. A more sudden fall in temperature is usually accompanied by sweating. A considerable amount of heat is lost from the body with the evaporation of the perspiration. In addition the heat-loss by conduction and radiation from the hyperæmic skin is increased.

In the acute infectious diseases the following stages are distinguished: **Incubation period** from the moment of infection to the appearance of the first manifestation of the disease; and among the exanthemata the **prodromal period,** marked by the first signs and symptoms prior to the eruption of the exanthem.

EXAMINATION BY MEANS OF RŒNTGEN RAYS

For the production of Rœntgen rays there is employed a high tension electrical current produced either by a large induction apparatus or by a high tension alternating-current transformer. The positive pole is connected with the anode of the tube and the negative with the cathode. The **cathode rays,** which are thrown off from the cathode, shaped like a perforated mirror, impinge upon the anticathode which is made of tungsten and set at an angle. From the anticathode is reflected a beam of Rœntgen rays. The Rœntgen tube is made air-free by evacuation; the more the tube is evacuated

the higher the strength of current necessary to activate it and the shorter the wave length of these so-called "harder X-rays." The harder rays have a much greater power of penetration while the softer rays, from a less completely evacuated tube, are easily absorbed by the soft parts and even by the skin. The latter are, therefore, employed principally in the therapeutic treatment of skin diseases, while in deep X-ray therapy, intended to affect the internal organs (e.g. the destruction of visceral neoplasms), hard rays must be used. For diagnostic transillumination hard or soft rays may be utilized according to the organ under examination. For the transillumination of the thorax and abdomen softer rays are employed since with harder rays the bones cast a shadow and the softer organs may cast no shadow whatever. The X-rays have the property of penetrating many solid substances which are impermeable to the other rays of the spectrum. In general the metals are the least permeable to the X-rays, the bones of the human body less so than the musculature, the heart and other air-free organs less permeable than the lungs. The X-ray is invisible to the human eye but may be made visible by the interposition of a screen impregnated with barium platinocyanide. Upon such a screen the X-rays produce a fluorescence which may be apprehended by the normal eye after it has become adapted to the darkness of a dark room. The X-rays act upon a photographic plate and it is thus possible to take pictures upon a plate interposed in their path.

In the examination of the trunk and the extremities the skeletal system may be clearly differentiated from the soft parts. Abnormalities of the bones, e.g. deformities, fractures, caries, tumors of the bones of the extremities or spinal column may be so diagnosed. Metallic foreign bodies, e.g. bullets or needles may be plainly brought into view. The introduction of a sound or of a barium mixture into the œsophagus makes possible the recognition of strictures or abnormal dilatations in its course. The heart appears in the Rœntgen picture as a pulsating shadow and by means of orthodiography or fluoroscopy may be more accurately outlined than by percussion. Concerning the measurements of the cardiac diameters see the chapter on Circulation. The topographically important lines: median line, mid-clavicular line, may be visualized by laying

over them a metal strip. The normal lungs appear clear and their borders, in contrast to the opaque liver, are usually sharp; it is thus possible to distinguish the position and the mobility of the diaphragm, a significant point in the diagnosis of pleurisy, emphysema, paralysis of the diaphragm, or subphrenic abscess. Any infiltration in the lungs casts a shadow as does any considerable pleural effusion. In the case of pneumothorax the affected side of the chest appears abnormally clear and the normal lung and bronchial shadows are missing.

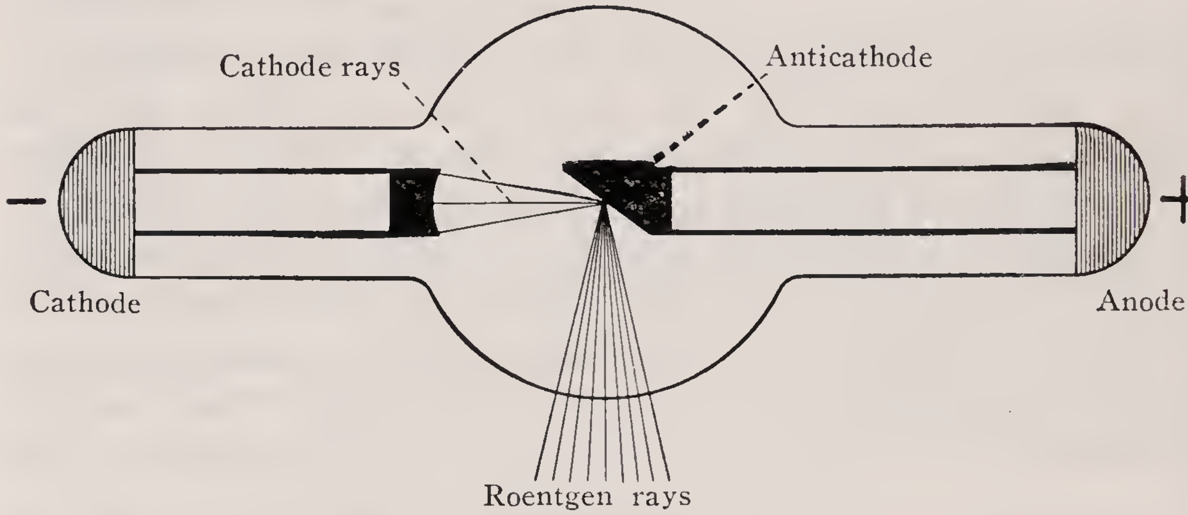

FIG. 1.—Roentgen ray tube.

Fluoroscopy of the thorax should be carried out not only in the sagittal direction, with the rœntgen tube behind and the fluoroscopic screen or photographic film in front of the patient (or vice versa), but also in a transverse and particularly in an oblique direction. Customarily two oblique positions are employed: the first, in which the right arm is elevated and the patient so rotated that the rœntgen tube is behind the left shoulder blade and the fluorescent screen lies against the right anterior axillary line, and the second, in which the x-rays pass from the right and behind to the left and forward. With the patient in the first oblique position one sees behind the shadow of the heart and in front of the shadow of the vertebræ a clear space corresponding to the posterior mediastinum. In this retro-cardiac space one sees the aortic arch bending toward the vertebral column and below this another space in which, if barium be swallowed, the œsophagus may be visualized coursing downward. In the case of tumors of the mediastinal glands this clear space be-

neath the aortic arch is replaced by an opaque shadow. Fluoroscopy is of particular value in the demonstration of substernal goiter or aortic aneurism; the latter appears as a pulsating shadow protruding from that of the aorta. Calcified arteriosclerotic vessels occasionally appear as dark strands. The X-ray also serves in the demonstration of stones in the kidney, ureters or bladder (phosphoric acid or calcium carbonate stones most easily visualized); gall-stones on the other hand, often fail to cast any distinct shadow. Significant information may also be obtained in cases of suspected inflammation in the paranasal sinuses. If the patient be caused to swallow a mixture containing barium sulphate the shadow cast by this opaque meal makes it possible to demonstrate the size and position of the stomach as well as its peristaltic movements; it is possible to see how long this meal remains in the stomach and in the course of the subsequent 24 hours to follow its course through the intestine and into the colon. Stenoses or other deformities of the stomach or intestine may thus be sharply outlined.

PERSONAL NOTES

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PERSONAL NOTES

CHAPTER II

RESPIRATORY ORGANS

THE EXAMINATION OF THE NOSE, PHARYNX AND LARYNX

RHINOSCOPY AND PHARYNGOSCOPY

The examination of the nose may be carried out either from the front by dilating the alæ nasæ with a speculum (anterior rhinoscopy), or from the back through the naso-pharynx (posterior rhinoscopy). Through the naso-pharyngoscope one sees medially the nasal septum, and laterally the lower and middle turbinates. Between the floor of the nasal cavity and the inferior turbinate lies the inferior, between the inferior and middle turbinates the middle, and between the middle and superior turbinates the superior nasal duct. The space between the middle turbinate and the septum is known as the olfactory portion, that between the floor of the nasal cavity and the border of the middle turbinate as the respiratory portion. The mucous membrane of the latter, covering the cartilaginous portion of the nose, consists of squamous epithelium. The upper portion of the nasal mucous membrane is covered with ciliated epithelium.

One particularly observes any deviation, erosion, ulceration, or perforation of the septum. Superficial ulcers on the anterior portion of the nasal septum are generally harmless except for the fact that they may lead to frequent epistaxis. Occasionally perforation of the cartilaginous septum may develop from such an ulcer (ulcus septi narium perforans). Perforation of the bony septum, as well as "saddle nose," indicates the presence of syphilis. Swelling and hypertrophy of the turbinates, or sometimes the presence of polyps, lead to nasal obstruction. Thin, watery pus discharged between the middle and inferior turbinates is often a sign of empyæma of the maxillary, frontal, anterior or posterior ethmoid sinuses. In ozæna the nasal cavity is strikingly wide, the turbinates and their mucous membranes and bones are atrophic and covered

with foul-smelling crusts (rhinitis atrophicans fœtida). A foul-smelling discharge from the nose also may be caused by caries (syphilitic) of the bony structures, by decomposition of pus in the sinuses, or by foreign bodies.

For posterior rhinoscopy a small mirror is used . . . similar to that employed in laryngoscopy, and set almost at right angles to the shaft. With local anæsthesia of the palate, the tongue is depressed with a spatula and the mirror passed in behind the uvula. The patient is directed to breathe as quietly as possible and then to say "Ha" in a nasal voice or to snore. The posterior border of the septum is first explored and then the turbinates. By drawing the mirror to one side the opening of the Eustachian tube and the groove of Rosenmueller are brought into view. By elevating the shaft of the mirror the roof of the naso-pharynx may be seen; lying upon this are the pharyngeal tonsils.

Hypertrophy of the pharyngeal tonsils and the adjacent lymphoid tissue produces so-called **adenoid vegetations.** These occur most frequently in children and may be so large as almost completely to obstruct the naso-pharynx, making breathing through the nose impossible. These soft masses are sometimes palpable to the finger introduced behind the soft palate.

The nose serves both for smell and respiration. The inspired air is warmed and saturated with moisture, and to a certain extent freed of its content of bacteria. If the nasal passages are obstructed or narrowed, the patient can only breathe through the mouth. The patency of the nose should be tested by obstructing one nostril and directing the patient to close his mouth and to attempt to breathe through the other nostril.

Mouth-breathing also leads to catarrh of the larynx and air passages and, at night, to loud snoring and restless sleep. Children, who, on account of adenoids, are accustomed to breathe persistently through the mouth, often show a stupid facial expression and diminished vivacity (Atrosexia nasalis). The hearing and development of the thorax in such children are sometimes also affected. Infection and inflammation of the middle ear (otitis media) more frequent in such individuals.

Disturbances of smell may be either central or peripheral in origin. Central anosmia occurs with lesions of the bulbus olfactorius (fracture of the skull, gun shot wounds, concussion of the brain), with brain tumors and tabes. Peripheral abnormalities of smell may appear with various diseases and particularly with atrophy of the olfactory mucous membrane.

The examination of the pharynx (pharyngoscopy) is accomplished by depressing the base of the tongue forcibly with a spatula while the patient holds the tongue in the mouth. One examines in succession the soft palate, the tonsils, and finally as much of the posterior pharyngeal wall as may be viewed through the mouth. In some cases of hypertrophic catarrh of the pharynx the lateral columns, extending from the posterior margin of the palate to the apertures of the tubes, are swollen.

One looks particularly for the presence of structural abnormalities, paralyses and defects of the palate (these latter are most frequently either syphilitic or congenital in origin), for inflammation, hypertrophy or atrophy of the pharyngeal mucous membrane, or paralyses of the pharyngeal muscles. The tonsils should be carefully examined to determine whether they are enlarged, ulcerated, abnormally reddened, covered with exudate or secretion, or finally whether they contain concrements (Angina lacunaris chronica). With paralyses of the muscles of the palate and posterior pharynx there occurs, in addition to difficulty of speech (see rhinolalia aperta), dysphagia with regurgitation of food or fluid through the nose.

EXAMINATION OF THE LARYNX

The larynx is possessed of three functions which, in disease, may be impaired either singly or jointly: (1) it is the organ of **voice production,** (2) it represents a portion of the **respiratory** tube, and (3) it plays an important part in the process of **swallowing,** particularly in preventing food from passing down into the trachea.

In the voice one differentiates **chest tones** and **head tones.** The chest tone is produced by the vibration of the vocal cords in their entire width. The head or "fissure" tone results when they vibrate only in their free margins. All vowels, diph-

thongs, and consonants are formed in the upper portion of the respiratory tract (mouth, pharynx, naso-pharynx and nose). With diminution in the intensity of the stream of air, as for example in emphysema, and in addition often with paralyses of the vocal cords, the voice is weak and faint. The monotonous voice lacks the tones in the upper and lower range; it is spoken of as husky when accompanied by adventitious noises. When the larynx for one reason or another can produce no vibrations and speech is possible only in a whisper the condition is described as **aphonia** or loss of voice. In functional or hysterical aphonia the usual noise is produced by coughing but the voice appears to have been lost, that is, the vocal cords function insufficiently with speech but otherwise are normal. **Mogiphonia** is characterized by easy fatiguability of speech. An abnormally deep voice is sometimes produced by inflammation of the vocal cords. **Double voice** or **diplophonia** occurs with unilateral paralysis of a vocal cord as well as with laryngeal polyps, which, in the process of phonation, may sometimes be caught between the vocal cords causing them to vibrate in segments and giving rise to a peculiar cracked voice. If the nasal passages are partially closed, e.g. in chronic coryza, or with tumors in the nose or naso-pharynx, the voice has the characteristic quality of nasal obstruction (rhinolalia clausa) in which m, n, and ng cannot be pronounced distinctly. If the closure of the nose from the mouth is incomplete (as in paralyses or perforations of the soft palate) there results the so-called **open nasal voice** (rhinolalia aperta) characterized by a persistent nasal quality and an inability to pronounce distinctly b, p, k, and t.

With severe inflammation and swelling of the larynx, most frequently in diphtheria, croup and œdema of the glottis as well as with tumors or paralyses of the dilators, or spasm of the constrictors, of the glottis, **respiration** is often considerably impeded (spasm of the glottis). The respiratory cycle is prolonged, particularly in the inspiratory phase, and is accompanied by a rough noise (stridor).

With stenosis of the larynx the head of the patient is thrown backward and the larynx rises and falls sharply with respiration. With tracheal or bronchial stenosis on the other

hand, the head is held forward and the larynx shows little or no movement during respiration.

Croup is a condition occurring particularly among children and most frequently at night, characterized by paroxysms of shortness of breath with stridor and a rough, barking cough. It is caused by an acute swelling of the mucous membrane beneath the vocal cords, and is usually not dangerous but tends to recur frequently. **Whooping-cough** is described in the chapter on Parasites and Infectious Diseases.

Spasm of the glottis occurs chiefly in infants and usually as a result of rickets with tetany (see Spasmophilia). These spasms may occur repeatedly in the course of a single day and the sudden spasmodic closure of the glottis may result in partial asphyxia. If the spasm subsides after a few seconds breathing is resumed noisily. **Functional spasm of the glottis** may sometimes occur at the moment when speech is attempted under conditions of extreme excitement with the result that the stream of air can scarcely pass through (Dysphonia spastica).

Difficulty in swallowing (**Dysphagia**) and severe pain radiating into the ear is associated with various ulcerative processes in the larynx, particularly with tuberculous ulcers of the epiglottis or about the arytænoid cartilage, but also with other types of inflammation of these structures.

Muscles of the Larynx

The **larynx is elevated** by the M. hyothyreoideus, depressed by the M. sternothyreoideus; the **epiglottis is raised** by the M. thyreoepiglotticus, **lowered** by the M. aryepiglotticus. Among the muscles which move the vocal cords themselves, the following are to be differentiated: 1. those which separate the vocal cords and thereby **widen** the rima glottidis (abductors); 2. those which draw the vocal cords together, thereby **closing** the rima glottidis (adductors); 3. those which **tighten** the vocal cords.

Widening of the rima glottidis is accomplished by the M. cricoarytænoideus posticus, which draws the processus vocalis of the arytænoid cartilage outward. **Closure of the rima glottidis** is brought about 1. by M. cricoarytænoideus lateralis (drawing the processus vocalis inward) and 2. by the

Mm. interarytænoideus (transversus and obliquus), approximating the bases of the arytænoid cartilage. **Stretching of the vocal cord** is accomplished 1. by the M. cricothyreoideus, which raises the cricoid cartilage against the lower border of the crico-thyreoid cartilage, thereby pushing the crown of the lamina of the cricoid cartilage backwards, 2. by the M. thyreoarytænoideus—musculus vocalis.

Nerves of the Larynx

The nerve supply of the larynx arises from the vagus. The **N. laryngeus superior** carries the motor supply to the M. cricothyreoideus as well as the muscles of the epiglottis, and the sensory supply to the mucous membrane of the entire larynx. **N. laryngeus inferior** (N. recurrens vagi), a purely motor nerve, courses downward in the vagus trunk along the carotid artery into the thorax, passes, on the right side, from behind forward around the subclavian artery, and on the left around the arch of the aorta, runs upward between the trachea and the œsophagus, and innervates all of the muscles of the larynx not supplied by the N. laryngeus superior. With regard to the nerve supply of the mouth and pharynx see the chapter on the Nervous System.

LARYNGOSCOPIC EXAMINATION

The patient is directed to open the mouth widely, to grasp the tongue, covered with a small piece of gauze, between the thumb and forefinger, and to draw it forward. The examiner then throws a bright beam of light into the pharynx by means of a head-mirror or head-lamp, inserts the laryngeal mirror (previously warmed over a lamp or in warm water) and presses it lightly against the uvula. By directing the patient to say "A" or "Ha" the epiglottis is caused to open and the anterior (in the mirror, upper) portion of the interior of the larynx is brought into view. For examination of the posterior laryngeal wall and the trachea (down to the bifurcation) the patient is directed to bend the head forward until the chin rests upon the manubrium sterni. The examiner kneels in front of the patient and looks almost perpendicularly upward into the mirror which occupies a horizontal position in the mouth of the patient. One sees, in the laryngoscopic picture: above,

(in front) the epiglottis, the aryepiglottic folds coursing downward (backward) to the arytænoid cartilage, the position of which is marked by the cartilagines Santorini visible as a small prominence. Slightly to one side of these are the cartilagines Wrisbergii. Between the arytænoid cartilages is the regio interarytænoidea. The interior of the larynx is divided into an upper (vestibulum laryngis), middle, and lower portion. The middle contains the two false cords (plicæ ventriculares); lateral to these lies the ventriculus laryngeus (pouch of Morgagni). The narrowest portion of the larynx is at the level of the free borders of the vocal cords, which form, with the processus vocales, the rima glottidis. The entire prism-shaped body, muscles and cords together, is called the labium vocale or true vocal cords. The ligamentum vocale, with the folds of mucous membrane which are reflected to cover the upper and lower surfaces of the vocal cords, is called the plica vocalis. The portion of the rima glottidis between the vocal cords is called the glottis ligamentosa or vocalis, that part between the two processus vocales is known as the glottis cartilaginea or respiratoria.

Direct laryngoscopy (**autoscopy** as described by von Kirstein) affords a direct view of the upper air passages from the mouth downward, the base of the tongue being pressed forward and the epiglottis opened. The examination is carried out with the physician standing behind the patient, who sits with the head bent sharply backward. A special, broad-grooved spatula is introduced and passed downward until its tip lies against the ligamentum glosso-epiglotticum medium, so that with gradual firm pressure the epiglottis and base of the tongue may be displaced forward. The examiner, then, with the aid of reflected or electric light, looking downward along the spatula, obtains a direct view of the interior of the larynx.

Direct **bronchoscopy** (described by von Killian) is accomplished by the introduction of a straight metal tube through the mouth into the larynx and through this into the trachea under adequate local anæsthesia. With electrical illumination one observes the bifurcation of the trachea and its division into the two primary bronchi. By shifting the tube into the

right or left bronchus one may examine the primary bronchi down to their division into the secondary bronchi.

Paralysis of the Vocal Cords

With paralysis of the **M. cricoarytænoideus posticus** the vocal cords cannot be drawn outward with respiration but remain near the mid-line. With bilateral paralysis the rima glottidis is narrowed to a slit, causing severe inspiratory dyspnœa. Voice production is, however, retained or only slightly impaired. A similar picture results from **spasm of the**

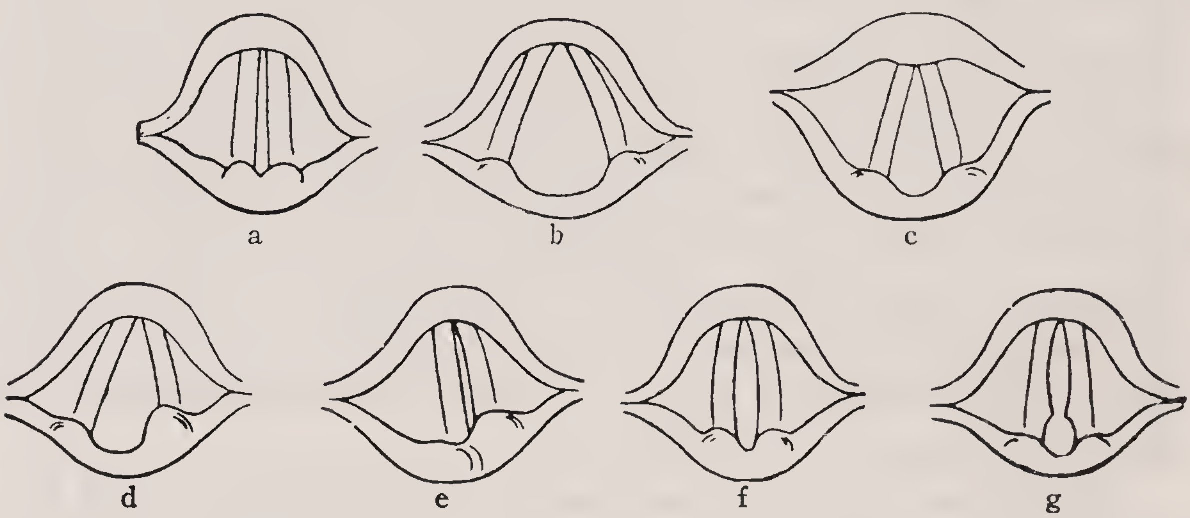


Fig. 2.

(a and b) Normal Larynx.
a. Position during phonation.
b. Position during respiration.
c. Cadaver position with bilateral recurrens paralysis.
(d and e) Leftsided recurrens paralysis.
d. Position during respiration.
e. Position during phonation.
f. Tensor paralysis.
g. Paralysis of thyreoarytænoidei and interarytænoideus.

adductors (Mm. cricoarytænoid. later. and interarytænoid.) and with bilateral ankylosis of the cricoarytænoid joint.

With **paralysis of the adductors** (Mm. cricoarytænoid. later. and interarytænoid.) the vocal cords cannot be drawn towards the mid-line; with bilateral adductor paralysis the rima glottidis remains open, forming a large triangle. Under these circumstances voice production is lost, coughing is toneless; respiration is unhindered.

With **paralysis of the M. interarytænoideus** the arytænoid cartilages can be approximated to their processus vocales (Mm. cricoarytænoid. later.), but not with their bases. There remains upon phonation, therefore, an open triangle in the posterior third of the rima glottidis.

With **paralysis of the M. thyreoarytænoideus** on one side the stretching of one vocal cord during phonation is incomplete, so that it remains concave at its free edge. With bilateral paralysis of this muscle the cleft of the glottis assumes a lancet shape (Fig. 2f). With coincident paralysis of the M. interarytænoid the glottis respiratoria remains open and the processus vocales project inward (Fig. 2g).

In unilateral **paralysis of the N. recurrens** the vocal cord on the affected side remains immobile during phonation and respiration (Fig. 2d). With phonation the unaffected vocal cord moves across the mid-line to meet the paralyzed cord, and the arytænoid cartilages cross (Fig. 2e). The arytænoid cartilage on the paralyzed side overhangs its fellow somewhat; voice faint. With bilateral recurrens paralysis both vocal cords remain immovable during phonation and respiration in the cadaver position, i.e., midway between the medium position of phonation and the abduction position of respiration (Fig. 2c).

With **paralysis of the N. laryngeus sup.** there results immobility of the epiglottis on the affected side, together with anæsthesia of the mucous membrane of the larynx. (Absence of reflexes and dysphagia.) In addition, on account of paralysis of the M. cricothyreoideus, the voice is rough and impure, and high tones cannot be produced.

With **paralysis of the N. vagus** there is, in addition to the paralytic phenomena dependent upon the paralysis of the Nn. laryng. sup. and recurrens, immobility of the musculature of the pharynx on the affected side—evidenced by the fact that the posterior pharyngeal wall is drawn toward the unaffected side during the act of swallowing.

With the paralysis produced by lesion of the N. recurrens the dilators of the glottis are earliest and most usually affected. With hysterical aphonia imperfect function of the **adductors** is present: On any attempt at phonation the vocal cords do not close, but the glottis remains open. Coughing, on the other hand, still produces a sound, indicating adequate closure of the glottis. Hysterical dysfunction of the larynx involves, in other words, only the function of speech and not that of coughing. In acute and chronic laryngitis partial paralysis of the vocal cords not infrequently occurs.

INSPECTION OF THE THORAX

One particularly observes whether the thorax is of normal contour, whether it is abnormally broad or narrow, particularly if the two halves of the thorax are symmetrical, and whether both sides move equally with respiration. In addition one determines whether the spinal column follows its normal course. Lateral bowing of the vertebral column, with the associated asymmetry of the ribs leads inevitably to differences in the percussion note over corresponding areas, which may often be mistaken for pathological dulness.

A pathological curvature of the vertebral column convex posteriorly is designated as **kyphosis.** If it is not bowed, but, as occurs with caries of the body of the vertebra, angular, it is designated as **gibbus.** Curvature of the spine, concave posteriorly, is called **lordosis;** and lateral deviation, **scoliosis.** Most frequently a curvature combines a deviation posteriorly and to one side, i. e., **kyphoscoliosis.**

Measurement of the thorax. In measuring the girth of the chest, the arms of the patient should be held horizontally away from the side and the measuring-tape so placed about the thorax that it passes posteriorly over the angles of the scapulæ and anteriorly below the nipples. The circumference should be measured at the end of full inspiration and after the greatest possible expiration. The girth of the chest should be in the neighborhood of one-half the height of the individual and the greatest respiratory excursion between five and eight centimeters.

In right-handed individuals the right half of the thorax may measure from a half to one and one-half centimeters more than the left; in left-handed persons there is a somewhat smaller difference in favor of the left side.

The sterno-vertebral diameter measures, in normal males at the level of the manubrium, about 16 cm., and at the lower end of the body of the sternum 19 cm. and the transverse diameter (diameter costalis) at the level of the nipple 26 cm. In females all these measurements are somewhat smaller.

Enlargement of one half of the thorax occurs with air or fluid in one pleural cavity, i.e. with pneumothorax and pleural effusion. **The enlarged side shows a diminution in the respiratory excursion,** and often obliteration of the intercostal spaces.

If there is a massive accumulation of fluid or air in one pleural cavity there may result an increase in circumference not only of the affected but also, to a lesser extent, of the sound half of the thorax, due to the fact that the mediastinum is displaced toward the healthy side and the normal lung is abnormally inflated.

Unilateral narrowing of the thorax takes place with shrinking of the lung (as a result of tuberculosis or chronic pulmonary disease) and, in addition, following the resorption of a pleural exudate, since the diseased and previously compressed lung cannot completely expand. One side of the thorax may be retracted by wide-spread pleural adhesions between the lung and chest wall. In this condition the anterior chest wall appears flattened on the affected side; **it fails to expand with respiration,** and the intercostal spaces are deepened. It is frequently possible to determine the diseased half of the chest by the fact that it takes less part in the respiratory movements.

Repeated measurements of the circumference of both halves of the thorax are particularly indicated in order to follow any increase or decrease in volume of a pleural exudate or pneumothorax.

Bilateral enlargement of the thorax occurs characteristically with **pulmonary emphysema.** The chest assumes a barrel-shape, appears short, and is apparently held persistently in an inspiratory position. The sterno-vertebral diameter is conspicuously increased. The neck is short. Enlargement of the inferior outlet of the thorax occurs with tumors or effusions in the abdominal cavity.

With **bilateral narrowing** the thoracic cage is long, flat and slender, the ribs course steeply backwards, the sterno-vertebral diameter is abnormally short, and the intercostal spaces wide. This type of chest is known as the paralytic thorax, and is frequently met with in pulmonary tuberculosis and habitus asthenicus.

MECHANISM OF RESPIRATION

The **normal respiratory rate** is from sixteen to twenty per minute in healthy adults, and forty-four per minute in infants.

The inspiratory enlargement of the thorax is brought about in men chiefly through descent of the diaphragm, less through elevation of the ribs; (Mm. scaleni, levatores costarum and intercostales externi). **Typus costoabdominalis.** In women it is often to a greater extent due to the elevation of the ribs. **Typus costalis.**

The **expiratory decrease in thoracic volume** is accomplished, under normal circumstances, principally by the elasticity of the lungs and ribs without the aid of muscles. The internal intercostal muscles may, however, come into play during expiration.

Inspiration and expiration are normally almost equal in duration and usually follow each other without any intervening pause.

The lungs themselves take no active part in the respiratory movements but follow passively the movements of the chest wall and the diaphragm.

In the healthy individual a small number of respirations per minute, of moderate depth, suffice for adequate gas exchange in the lung. The rate and depth of the respiratory movements are governed by rhythmic impulses from the **respiratory center** in the medulla. This center is susceptible of influence by chemical and nervous factors.

The **chemical control of breathing** is effected by the sensitivity of the respiratory center to the carbon dioxide content or hydrogen ion concentration, or oxygen tension in the blood supplied thereto. Increase of the first two factors or decrease of the third is accompanied by more rapid or deeper respiratory movements.

The **nervous control of breathing** is in large measure the result of certain reflex influences originating in the lungs and proximal portion of the aorta passing to the midbrain via afferent fibers of the Nn. Vagi.

Dyspnoea,* or labored breathing, is distinguished by subjective discomfort (breathlessness) on the part of the patient.

It may result from excessive chemical stimulation of the respiratory center by the accumulation of carbon dioxide in the blood or from reduction of vital capacity in proportion to the required volume of ventilation. It is a conspicuous symp-

* See Burwell, C. S.: International Clinics, Vol. II, series 43, p. 43.

tom of circulatory insufficiency and of certain types of pulmonary disease. (Ed.)

One distinguishes **inspiratory** and **expiratory** dyspnœa. In the former inspiration is particularly difficult; it is accomplished only with great effort and with the aid of the **accessory muscles of inspiration** (Mm. sternocleidomastoideus, pectoralis major and minor, trapezius, serratus anterior, the extensors of the spine, the dilators of the nose, mouth and larynx). If, in the case of severe inspiratory dyspnœa, there is coincident stenosis of the air passages or insufficient capacity of the lung an inspiratory retraction may be seen in the region of the xiphoid process and the lower ribs.

In **expiratory dyspnœa** the contraction of the thorax is accomplished with difficulty and the duration of expiration is prolonged in comparison to inspiration. The auxiliary muscles are brought into play (the abdominal muscles and the M. quadratus lumborum). Expiratory dyspnœa is persistently present with **pulmonary emphysema** and temporarily so in **bronchial asthma.** Dyspnœa may sometimes be both inspiratory and expiratory.

Asthma may be defined as paroxysmal shortness of breath. In **bronchial asthma** short or protracted periods of severe dyspnœa alternate with periods of complete well-being. During the attack the bronchi are narrowed by spasm, the diaphragm is persistently depressed and the lungs inflated. Sonorous and whistling râles are audible over the chest and there is expectorated tenacious sputum, the characteristics of which will be described later. Dyspnœa occurring during heart disease or nephritis is denoted as cardiac or uræmic asthma. Hay asthma is characterized by attacks of shortness of breath (accompanied by symptoms of irritation of the nose and conjunctivæ) following exposure to the pollens of various types of grass.

Paroxysmal Cardiac Dyspnœa: With certain types of cardiovascular disease, notably syphilitic aortitis, dyspnœa may occur in paroxysms. More frequent at night such attacks may waken the patient from sleep. No entirely adequate explanation of this phenomenon has been offered but the rapidity of onset suggests that reflex, rather than chemical,

stimulation of the respiratory center is the most important factor in precipitating the attack.

Cheyne-Stokes respiration is characterized by periods of complete cessation of respiration (apnœa) alternating with periods during which the respiratory excursions become progressively greater and greater and then gradually decrease in amplitude. This phenomenon is present in many cases of severe intracranial disease, in heart disease, in uræmia, in various types of poisoning, e.g. after morphine or veronal. In the healthy individual during sleep or at rest a periodic increase and decrease in the depth of respiration may take place, and in children and elderly individuals, or in exhaustion, there may sometimes occur genuine periods of apnœa.

To a type of respiration occurring characteristically in diabetic coma **Kussmaul** gave the name **"air hunger."** In this condition the breathing of the semi-conscious or comatose patient is persistently abnormally deep and noisy.

Spirometry

The vital capacity is that volume of air which can be expelled by the deepest possible expiration following the fullest possible inspiration. In healthy males it amounts, on the average, from 3500 to 5000 c.c.; in females, 2500 to 3700 c.c. It is roughly proportional to the height of the individual. The vital capacity is diminished in children and in the aged, in the presence of disease of the respiratory system, and after a meal which fills the stomach.

The complementary air is that volume which can be inspired after a normal inspiration = 1500–2500 c.c.

The reserve air is that volume which can be expired by the deepest possible expiration following a normal expiration = 1500–2500 c.c.

The tidal air is that volume which is ordinarily inspired and expired during quiet respiration = 500 c.c.

The residual air is that volume which remains in the lungs following the deepest possible expiration = 1000–1500 c.c. The total volume of air within the lung after a deep inspiration is therefore in the neighborhood of 6 liters (residual air plus vital capacity).

Mid-capacity is defined as the volume of air present in the

lung between in- and expiration during normal quiet breathing; it is equivalent to residual air plus reserve air plus one half the tidal air. The mid-capacity, i.e. the average amount of air within the lung, increases with stimulation of respiration, e.g. with exercise, with all types of dyspnœa and with the shortness of breath of cardiac failure. Under these circumstances, and also in pulmonary disease, the residual air is increased at the expense of the vital capacity.

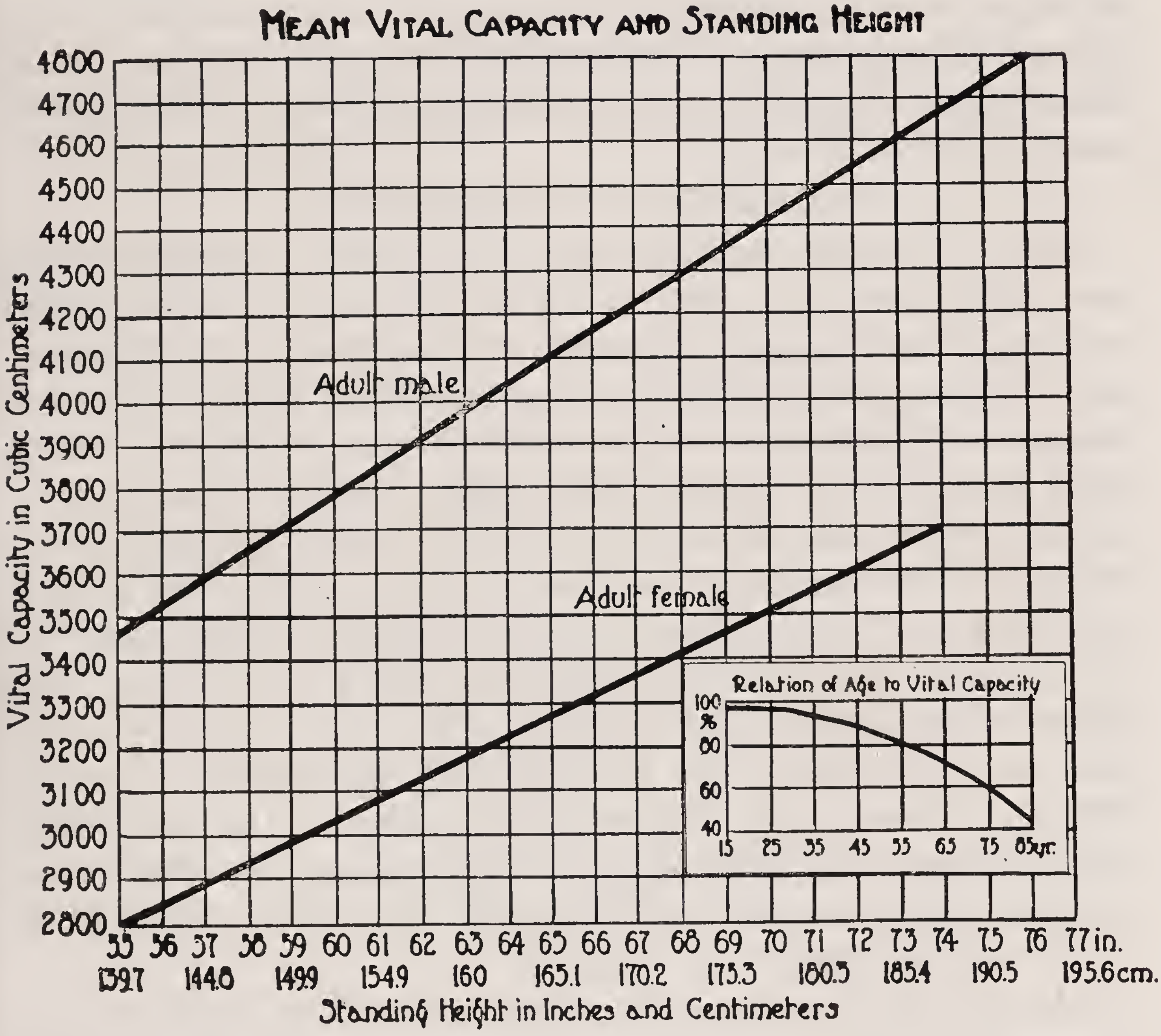


CHART I *

Vital capacity is measured by means of a spirometer. The patient is directed to inspire as deeply as possible and then to blow out as much air as possible into the instrument. Determination of the total volume of air inspired and expired over a long period of time involves the use of some type of gasometer.

The atmospheric air has a relatively constant composition;

*Reproduced by permission of Dr. G. E. Fahr.

nitrogen 79%, oxygen 20–21% and carbon dioxide about 0.04%. **The expired air** is considerably richer in carbon dioxide (approximately 4% CO_2), poorer in oxygen (about 16% O_2), and is saturated with water vapor. The amount of carbon dioxide and, in part also, of water in the expired air varies according to the processes of combustion in the body. It is least during hunger and at rest, and increases proportionately following the taking of food, **during activity,** and in addition, under conditions of increased heat production, e.g. in fever. The amount of carbon dioxide expired per day, upon the average diet and at rest, is about 900 grams, with exercise 1200 grams or more.

PERCUSSION OF THE THORAX

By the impact of the percussing finger or hammer the chest wall is set into vibration. These vibrations are imparted to the surrounding air and impinge upon the ear of the examiner. Their type and intensity are dependent in part upon the intensity of percussion and in part upon the resonance of the chest wall. If the wall of the thorax itself is heavy, or is covered by a thick layer of fat or heavy musculature, it produces, even with vigorous percussion, a less intense sound than a thinner chest wall. Thus the percussion note is less loud over the shoulder blades, and the muscles which cover them, than above the scapulæ. If the muscles of the chest wall and abdomen are contracted, e.g. by coughing, in bearing down, or lifting, its ability to vibrate is reduced and the percussion note is correspondingly soft. For this reason one should not percuss the chest of a child while it is crying or that of an adult at the moment of coughing.

Above all, the type of vibrations of the chest wall is dependent upon the ability of the organs contained therein to vibrate. The percussion blow delivered against the chest wall is transmitted to these organs and induces in them their characteristic vibrations. These cause the chest wall to vibrate in harmony and are thus transmitted to the ear of the examiner. If beneath the chest wall there is air-containing, resonant lung, or air-containing stomach or intestine, or, as in the case of pneumothorax, an air-filled space, the percussion note is loud, of long duration, and, dependent upon the size and character of the region percussed, may be low or high in

pitch. If, on the other hand, there lies beneath the chest wall a substance which contains no air and is therefore incapable of being set into vibration, as, for example, the heart, liver, consolidated lung or an effusion of fluid, the chest wall vibrates scarcely at all upon percussion for the reason that, on the one hand, its vibrations are dampened, and, on the other, the sympathetic vibrations of the organs within are lacking. The resulting note is dull, of short duration, and usually of higher pitch. With heavy percussion the effect of the percussion stroke penetrates more deeply into the interior of the chest. The quality of the percussion note so elicited is dependent chiefly upon those organs or portions thereof which lie nearest the chest wall. An **air-free** organ, a tumor or area of consolidation which is separated from the inner surface of the chest wall by more than 5 cm. and is covered by air-containing lung, produces no changes in the percussion note and can therefore not be outlined by this method. In general, therefore, percussion furnishes information only concerning the resonance of organs beneath or near the chest wall. If, however, there lies beneath an organ which is next to the chest wall (e.g. the lung, heart, liver or spleen), an **air-containing** and therefore resonant space, such as stomach or intestine, this may be set in vibration by vigorous percussion and produce a tympanitic note. Lighter percussion, on the other hand, will scarcely reach a space lying so far beneath the surface. This explains the fact that the heart, which may in part overlie the air-containing stomach, may give a tympanitic note upon percussion, as well as the fact that its boundaries may only be accurately outlined with relatively light percussion.

If, immediately within the chest wall, there lies a thin sheet of air-containing lung (not over 5 cm. in thickness) and beneath it an air-free non-resonant organ, e.g. the heart, or liver, this **thin** sheet of lung gives a higher, shorter, and sometimes less resonant percussion note than a thicker sheet of lung tissue. It is this phenomenon which makes it possible to determine the "relative" cardiac and liver dulness.

In percussion one distinguishes the following qualities of the note:

Loud or soft (clear or dull);
Long or short (full or empty);

High pitched or low pitched;

Bell-like or not bell-like (tympanitic or not tympanitic). One may also distinguish a special metallic quality in the note, determined by the presence of very high overtones.

Differences in intensity, i.e. in the amplitude of the vibrations which impinge upon the ears, are classified as **loud** or **soft.** This difference is primarily dependent upon the resonance of the organ percussed, particularly upon its **content of**

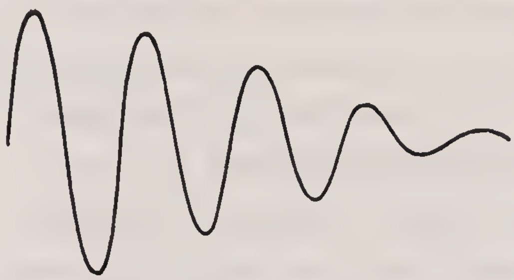


Fig. 3.—Loud note.

Fig. 3a.—Soft note.

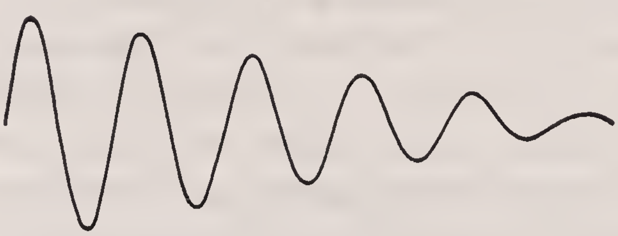


Fig. 4.—Long note.

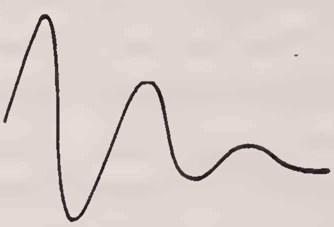


Fig. 4a.—Short note.

Fig 5.—High note.

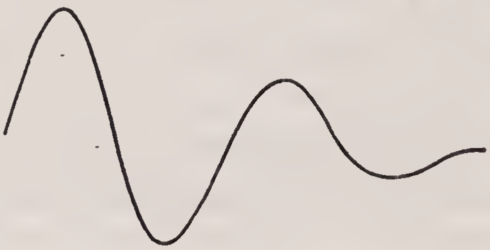


Fig. 5a.—Low note.

air, and secondarily upon the force of the percussion blow. In examining different areas, therefore, it is necessary to percuss with equal intensity in order to avoid apparent differences in the note which are in reality due to differences in force of the blow. Inequalities in percussion elicit inequalities in note which may easily be mistaken for signs of disease. As **Skoda** insisted, percussion is at best comparative; it serves only to show whether the notes elicited at two points are alike or unlike.

Auenbrugger, the inventor of percussion, used the terms "clarior," i.e. "distinct" for the loud note over the lungs, and "obscurior," i.e. "indistinct" for the soft note over air-free organs. Skoda translated "clarior" as "clear" and "obscurior" as "dampened" or "dull." It is important to note that these expressions "clear" and "dull" are employed clinically in a sense quite different from that of ordinary speech. Here

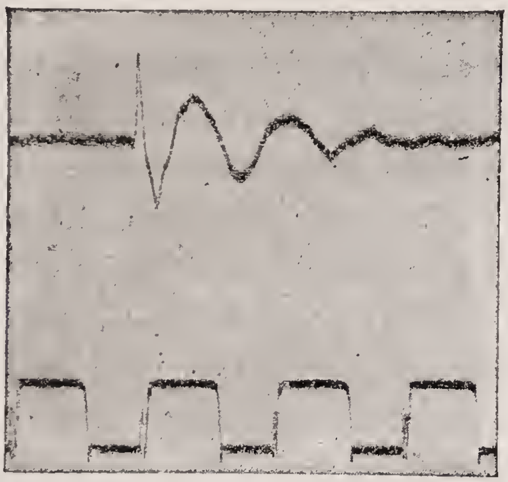


Fig. 6.—Normal, loud, low note of the lung. (Lower curve time-marker in 1/50 second.)

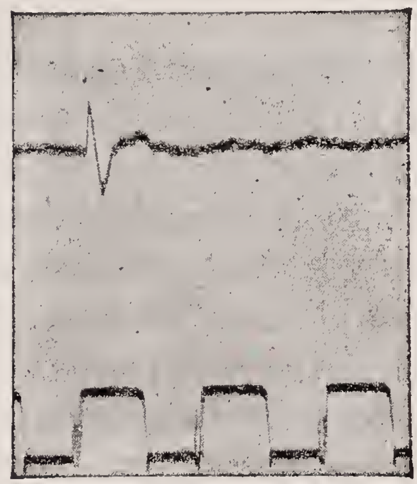


Fig. 7.—Very soft, short, dull note over a large pleural exudate.

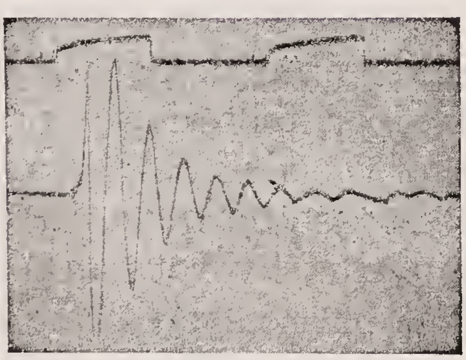


Fig. 8.—Tympanitic note over abdomen, recorded with a condenser microphone and oscillograph. Regular sine curve with 208 vibrations per sec.

"clear" is often synonymous with a high and "dull" with a low note, whereas Skoda used these terms to denote loud and soft.

Over the normal thorax and abdomen a loud note is produced in the region of the lungs, the stomach and intestine; a dull note is elicited wherever the heart, liver, spleen and kidneys are in contact with the chest or abdominal wall. A very dull or a **flat** note is obtained over the musculature (absolute dulness). The air-free, soft tissues, such as the liver, heart and

musculature, vibrate scarcely at all upon percussion, and one hears, therefore, only the pat of finger against finger or of hammer against pleximeter. Air-free solid tissues, i.e. the bones of the spine, serve simply to transmit the percussion blow. Percussion over such tissues may, therefore, set into vibration adjacent organs and thereby elicit a tone. This serves to explain the relatively loud note obtained upon percussion of the spine or the sternum in the region of the lungs.

A **soft** note (dulness)[1] in the region of the lungs occurs: (1) If that portion of the lung lying next to the chest wall contains no air; (but the air-free portion must be at least 3–4 cm. in diameter and lie adjacent to or near the chest wall). Air-free tissues which lie deeper than 5 cm. within the chest and are covered by air-containing lung produce no impairment of the percussion note. A central pneumonia or a tumor or aneurysm lying deep in the thorax is, therefore, not to be made out by percussion.

The parenchyma of the lung may be air-free: (a) due to **infiltration** in pneumonia, tuberculous infiltration of the lung, hæmorrhagic infarction, abscess, or neoplasm; (b) due to **atelectasis.** As atelectasis one designates a condition in which the alveoli contain no air and their walls are collapsed. It may be produced through compression of the alveoli by a pleural or pericardial exudate, or, following the occlusion of a bronchus, by absorption of the air from the alveoli in its domain.

(2) **If fluid is interposed between the lung and chest wall** (pleural effusion, empyema, hydrothorax). Fluid in the pleural cavity gives rise to a particularly soft and short (so-called flat) note. The accumulation of fluid must reach a volume of 400 cc. in adults before it is demonstrable. Thickened pleura or tumors may also interfere with the resonance of the chest wall and produce dulness.

In the absence of pleural adhesions exudate in the pleural cavity tends to collect in the lateral and posterior inferior portion and to spread anteriorly and upward. The superior

[1] The expression, "dulness," should connote a soft note (e.g. cardiac dulness, dulness over a pleural exudate); however a dull note is not only less loud, but also less deep, that is somewhat higher in pitch and at the same time shorter in duration. The expression, "dulness," is used in a different sense in medicine than in physics where it denotes simply a sudden reduction of vibrations.

margin of such pleural exudate assumes a curve which is highest in the posterior axillary line and falls toward the spine and the anterior chest wall (the parabolic curve of **Damoiseau** and **Ellis**). With massive pleural effusion there is present on the sound side posteriorly and adjacent to the spine a three-cornered area of dulness, the so-called paravertebral triangle. There is also dulness to percussion over the spine in this region.

With an inflammatory exudate the borders of dulness change little or not at all with **change in position** of the patient, since the exudate is, so to speak, encapsulated by the cohesion of the two pleural layers. With hydrothorax, which is frequently bilateral, though the level of dulness may not be equally high on both sides, the fluid level may change somewhat, but usually only after a quarter or half hour in a given position. If both air and fluid be present in the pleural cavity (**pyo-** or **hydropneumothorax**) the fluid level immediately assumes the horizontal position, e.g. with the patient erect the fluid is demonstrable in the anterior inferior portion of the thorax; with the patient on his back however, it sinks posteriorly leaving a tympanitic area in front. Above massive pleural exudates the percussion note is usually high-pitched and tympanitic; above less massive effusions the note is often loud and deep. With massive accumulation of air or fluid in the pleural cavity the mediastinum and heart are displaced toward the sound side and the diaphragm is pressed downward.

(3) Finally, a dull percussion note is elicited wherever intrathoracic tumors lie against the chest wall (tumors of the lung, of the pleura or glands, or aneurysms of the aorta).

Retrosternal enlargement of the thyroid (struma substernalis), enlargement of the thymus, or of the lymph glands in the anterior mediastinum above the heart and aorta, result in dulness over the manubrium and the adjacent portions of the first and second intercostal spaces. Tumors of the lymph glands at the hylus, e.g. enlargement of the bronchial lymph glands in tuberculosis, are rarely demonstrable by percussion since these glands lie deep in the thorax in front of the spine, the aorta and the bifurcation of the trachea (see fig. 20). Large tumors of the lung hylus (carcinoma, granuloma), as

well as aneurysms of the aorta, may be overlooked upon percussion, particularly when they do not approach the chest wall. These may be demonstrated often only with the X-ray. Dulness over the interscapular space, or over the spine from the 2nd to the 5th thoracic vertebra, is an unreliable sign of tuberculosis of the bronchial lymph glands, and is more often dependent upon the thickness of the trapezius and rhomboid muscles.

Long or **Short.** As a "full" (sonorous) note Skoda designated one given by a large resonating body, e.g. a large bell, the ring of which persists for some time. A short note would therefore be produced by a small body, the vibrations of which fall away and disappear rapidly. The **vibrations of a long note persist longer.** The percussion note of the healthy air-containing lung is, similarly, of longer duration, whereas that of air-free tissue, e.g. infiltrated lung, musculature, or pleural effusion, is shorter. In the human body the difference between the full and short note is sometimes not sharp but still demonstrable. The full note of the normal lung has been shown to possess not only a considerably greater amplitude of vibrations but also a duration of approximately twice the length (0.42 sec.) of the short note over infiltrated lung or muscles (0.28 sec.). The percussion note is, moreover, full, i.e. ringing, when it is made up largely of **low** tones, since such tend to fade away more gradually. This is the explanation of the particularly full and ringing note present with pulmonary emphysema and pneumothorax. It is incorrect to use the expression "short" as synonymous with "dull," i.e. soft. For example, in the case of tuberculous infiltration of one pulmonary apex the note over this region is not only dull but also higher in pitch and shorter in duration than that over the sound apex.

High- and **Low-Pitched.** The pitch of a note is determined by the frequency of its vibrations per second; the greater the frequency the higher the note. The percussion note presents in a physical sense a **noise** made up of a mixture of individual tones. It has been shown that, in the case of the note of the normal lung, this series of tones extends from the middle to the great octave, i.e. to the deepest tone usually reached by a bass voice. The deep, fundamental tone of the lungs (about 120

vibrations per second) is best elicited by percussing a soft rubber plessimeter (such as an eraser) laid against the chest wall with a thick rubber hammer (reflex hammer).

The percussion note over the healthy lung of adults includes lower tones (120 vibrations per sec.) than that in children (about 170 vibrations per sec.). The lowest series of tones is elicited over an emphysematous lung, or a pneumothorax (75 vibrations per sec.). With infiltration of one apex, e.g. in tuberculosis, these low tones are lacking, while over the apex of the other healthy lung they are present. As a result the percussion note on the diseased side appears higher or, more correctly, less low in pitch. Among the tones which are included in the percussion note of the lung the lowest tend to be most characteristic and to persist the longest. A percussion note which includes very low tones is therefore loud and of long duration. Differences in pitch of the percussion notes and particularly of the lower tones are better appreciated with the aid of certain types of resonators than with the naked ear since the human ear is far more sensitive to high tones than to low. The pitch of a percussion note is most easily distinguished when one of its component tones is particularly loud, as is the case with the so-called tympanitic note.

The various phenomena designated as "Changes in Pitch" are related to the pitch of this fundamental note. **Wintrich's Change in Pitch** is characterized by a tympanitic percussion note whose pitch alters with **opening and closing of the patient's mouth.** This may be imitated if one percusses one's own larynx or cheek and at the same time opens and closes the mouth. It is present over pulmonary cavities, **provided these are in open communication with a bronchus,** and also occasionally in pneumonia and above massive pleural exudates, when consolidated tissue immediately overlies a bronchus.

Bell-like or **tympanitic** percussion note is distinguished from the non-tympanitic in that the former is of distinguishable pitch and is apparently a much purer tone. The tympanitic note is characterized by the simplicity and regularity of its vibrations, wherein it approaches a pure tone in the physical sense (see fig. 8). The non-tympanitic, on the other hand, is a complex note indicating that it is compounded of various

non-harmonious vibrations (see fig. 6). The tympanitic note is usually higher in pitch (in the octaves c–c′). It occurs over large air-containing cavities (i.e. larynx and trachea) and over the air-filled stomach or intestines. The normal lungs in the thorax, on the contrary, do not give a tympanitic note except over the lower portion of the left lung (overlying the stomach) where one may elicit a tympanitic note with vigorous percussion by setting into vibration, through the thin lung border, the air space of the stomach immediately below the dome of the diaphragm.

A **tympanitic percussion note** occurs in the following **abnormal conditions:**

(1) With consolidation of the lung tissues, making possible, in reality, the percussion of the bronchi, which normally are filled with air, e.g. over pneumonia, compressed-lung or other atelectases.

(2) In the presence of **pathological** air-containing cavities:

Cavities with rigid walls surrounded by infiltrated lung tissue, if these cavities lie close to the chest wall.

Sometimes with **pneumothorax,** when the volume of air is small, or the pneumothorax open. With large, closed pneumothorax, i.e. with extensive accumulation of air in the pleural cavity, the percussion note is always abnormally deep, loud and **not tympanitic.**

(3) With **relaxation of the lung,** in the neighborhood of an extensive **infiltration** or of pleural or pericardial **exudates.** So, for example, one may elicit a high-pitched tympanitic note over the upper lobe in the presence of pneumonia of the lower lobe on the same side, or above a massive pleural effusion. The lung removed from the thorax after death is collapsed and gives a typical tympanitic note (about 220 vibrations per sec.). A tympanitic note also occurs sometimes with **partial consolidation** of the lung tissues when both air and fluid are contained therein, e.g. in the first and second stages of lobar pneumonia, and in bronchopneumonia.

A metallic ringing percussion note depends upon the occurrence of very high overtones (of several thousand vibrations per sec.) together with a low fundamental tone, and upon a slow reduction in intensity. It arises in large air-containing cavities with smooth walls. One encounters this

metallic ring upon percussion over the stomach or intestine distended with gas. The sound may be imitated by striking with the finger nail a small rubber ball held against the ear, or by the ring of a silver coin or the striking of a small clock. Such a metallic ring is elicited over the thorax: In the presence of large **smooth-walled cavities** of not less than 4 cm. diameter; with **pneumothorax.**

The metallic ring characteristic of large, smooth-walled, air-containing cavities is only seldom to be elicited by the ordinary methods of percussion, since the high overtones are too faint to penetrate the chest wall. Practically it is only heard when either the ear or the stethoscope is pressed directly against the chest wall during percussion. Moreover, this type of note may be brought out more often by percussing, not with the finger or rubber hammer, but with some hard substance such as a pencil, upon a plessimeter laid against the chest.

The so-called "Signe du Sou" or **"Coin Test"** is elicited by placing a large coin against the chest wall and striking it with another. If, now, one listens over an adjacent portion of the chest or better over the opposite wall of the same half of the thorax, one hears the clicking of the coins, sometimes ringing, sometimes faint over consolidated compressed lung, or actually tinkling over pneumothorax or cavities.

Vigorous percussion, causing the air to be pressed out of a cavity through a narrow orifice, may elicit a noise similar to that given by a **cracked pot.** Occasionally, in healthy individuals, and particularly in children, a cracked-pot sound is elicited by percussing during speech or crying. Under pathological conditions it is present over superficial cavities, which are connected by a narrow opening with a bronchus, and sometimes over relaxed or infiltrated lung (pneumonia and pleural effusions). The **"cracked-pot"** sound may be more apparent if the patient opens the mouth.

Percussion of the Normal Lung

The upper border of the lung (pulmonary apex) lies anteriorly 3 to 4 cm. above the upper margin of the clavicle, and posteriorly at the height of the spinous process of the seventh cervical vertebra; its position does not change with

inspiration or expiration. The upper portion of the lung, lying in front beneath the infraclavicular fossa, and, in back, beneath the supra- and infra-spinous fossæ gives normally a softer note than the lower portion for the reason that it is covered with a thicker layer of muscle. Comparison of the note of the upper portion of the lung with that of the lower is therefore of uncertain value.

The lower lung margin lies at the sternal border beneath the sixth rib, in the right mammillary line usually beneath the lower border of the sixth or the upper border of the seventh, in the anterior axillary line at the lower border of the seventh, in the scapular line beneath the ninth rib, and next to the spine at the level of the spinous process of the eleventh thoracic

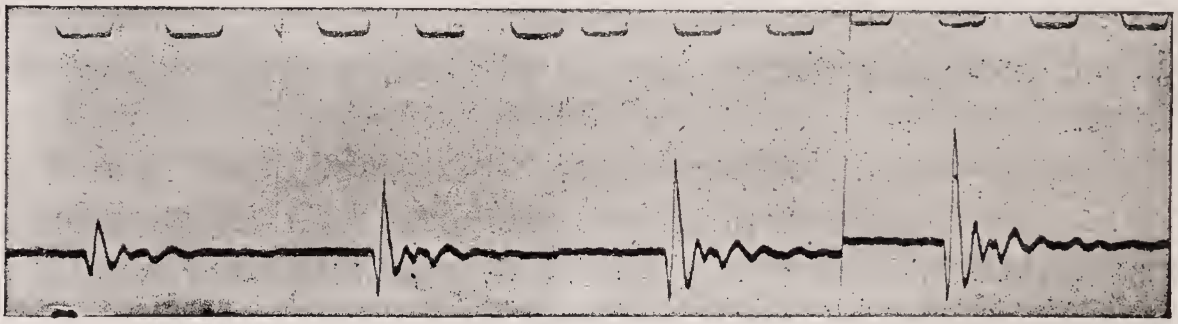


FIG. 9.—Percussion over right lower lung border during inspiration. The soft note of the liver is replaced by the loud note of the lung as the lung margin descends with inspiration. As shown in the sound records the amplitude and duration of the vibrations increases as the lung descends.

vertebra. On the left side next to the sternum the anterior margin of the lung coincides with the absolute cardiac dulness. The border of the left lung lying over the stomach may not be percussed accurately since, in this region, there is a **gradual** transition from the **non-tympanitic note** of the lung to the loud **tympanitic note** of the stomach.

To percuss the **pulmonary apex** the examiner stands behind the patient who sits upon a stool or bed with his head bent forward and arms folded in front. One compares first the note in the supra-clavicular and supra-spinous fossæ on the two sides, and, by percussing along the border of the trapezius muscle upward to the neck, locates the position of the pulmonary apex. This may also be located by determining the boundary between the normal lung note and the soft or tympanitic note of the neck muscles and underlying trachea. Retraction of one lung apex may occur with shrinking as a result of tuberculosis. One proceeds then with percussion,

comparing always symmetrical areas on the two sides, examining both lungs in front and in back, and determines finally the position of the lung bases. To locate the **lower borders of the lungs** one percusses downward in the right mammillary line and determines the point at which the pulmonary note, which becomes softer and higher pitched below the fifth rib, passes over into the dull note of the liver, i.e. where the last trace of the characteristic note of the lung disappears. In a similar fashion one then percusses out the lower border of the lungs at the right sternal margin and in the scapular lines.

Topography of the lobes of the lungs: The fissure between the upper and lower lobes begins posteriorly on both sides at the level of the third or fourth thoracic vertebra (first or second dorsal spine). It courses downward and laterally ending on the left side in the mammillary line at the level of the sixth rib. On the right it divides at a point approximately six cm. above the angle of the scapula into an upper and lower branch, which include between them the middle lobe. The upper branch runs almost horizontally and reaches the anterior margin of the lung at the level of the fourth or fifth costal cartilage. The lower branch, which separates the middle from the lower lobe, passes steeply downward and reaches the lower border of the lung in the mammillary line. Above the fourth rib, in back, therefore, one percusses only the upper lobe, from there downward the lower lobe; in front on the left side only the upper lobe, on the right side down to the third intercostal space upper lobe, from here downward middle lobe, and in the right axilla upper, middle and lower lobes.

With quiet respiration the lung borders are displaced only slightly. In the prone position the anterior lower lung border is about two cm. lower than in the erect position. In lateral decubitus the lower border of the lung on the side uppermost sinks about three cm. in the axillary line. With deep inspiration the respiratory excursion of the lung border may be greater and in the case of deep inspiration with the patient on his side the lower border of the lung on the upper side may move nine cm. The greatest respiratory excursion of the lung takes place in the axillary line (filling of the complementary space).

Depression of the lower lung border is persistently present in pulmonary emphysema, and temporarily so in asthmatic attacks.

Elevation of the lower lung border occurs bilaterally with any displacement of the diaphragm upward by accumulation of fluid (ascites), tumors or unusual accumulations of fat in the abdominal cavity, and in pregnancy. Elevation of the lower border of the lung **on one side** takes place with any process involving shrinking of the lungs and pleura.

The respiratory excursions are diminished in emphysema and chronic passive congestion of the lung (unilateral with stenosis of a bronchus), as well as in early pleurisy, and are absolutely lacking if the lung be adherent to the chest wall.

AUSCULTATION

The Breath Sounds

Breath sounds are classified as:

Vesicular = alveolar.
Indeterminate = broncho-vesicular.
Bronchial = tubular, and
Metallic = amphoric.

In addition the breath sounds may be:

Of normal intensity,
Abnormally loud (increased), or
Abnormally faint (diminished).

Vesicular breathing (alveolar breath sounds). Over the normal, healthy lung one hears, during inspiration, a low shuffling or rustling sound and during expiration a similar sound of very short duration or no sound at all. The sound of vesicular breathing can be imitated by holding the lips in the position for pronouncing O or U and gradually drawing in and blowing out air through this opening. The respiratory murmur is simulated by the rustling of a breeze in pine trees. It is made up of many component tones of a frequency of 100 to 1,000 per minute, among which those of a frequency of 100 to 200 per minute possess the greatest amplitude and hence determine the relatively low pitch of the vesicular breath sounds. It is present only over air-containing, normally-functioning lung tissue, and when heard over the chest

Fig. 10.—Vesicular breath sounds, recorded by means of condenser-microphone and oscillograph. Fundamental tone 120 vibrations per sec.; overtones about 500 vibrations per sec.

Fig. 11.—Tracheal breath sounds, recorded in same fashion. 500–600 vibrations per sec.

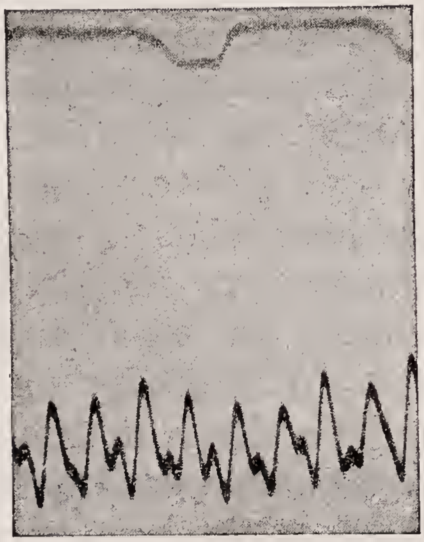


Fig. 12.—Bronchovesicular breath sounds. 200–500 vibrations per sec.

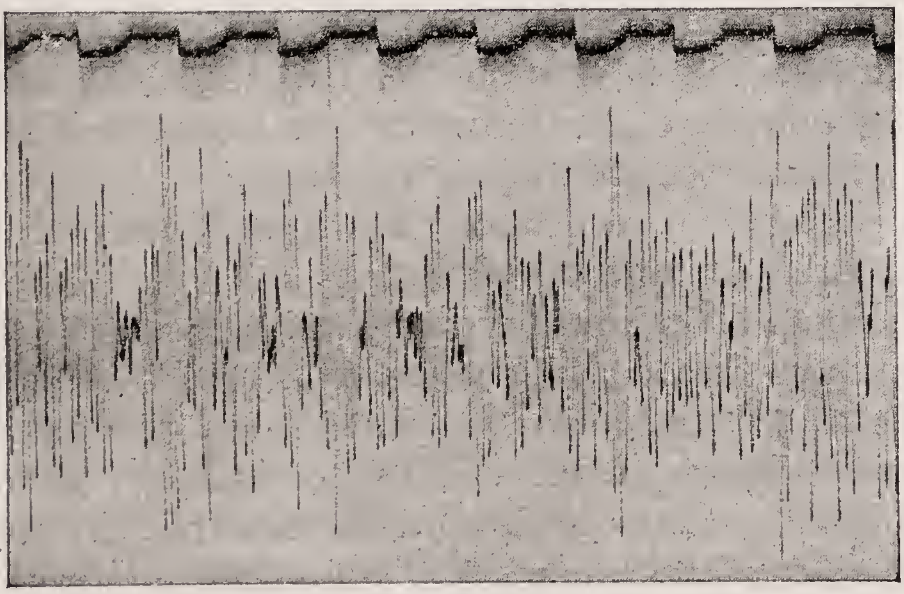


Fig. 13.—Bronchial breath sounds. 1000 vibrations per sec.

wall is positive evidence that air-containing lung, which is taking part in respiration, lies immediately beneath.

Vesicular breath sounds are only faintly heard during quiet breathing; with deeper respiration they become louder, (without otherwise changing their character). Their intensity is directly proportional to the inflatability of the lung. Vesicular breathing is therefore **diminished** over any portion of the lung which, as result of disease, has lost the ability to inflate with inspiration and to deflate with expiration, or wherever, on account of narrowing or occlusion of the bronchi, the inspiratory filling of the corresponding section of the lung is impeded or rendered impossible. One hears no breath sounds, sometimes, in asthma or severe bronchitis over certain circumscribed portions of the lung, for the reason that the afferent bronchus is plugged with secretion. Similarly, the closure of a bronchus by neoplasm or foreign body results in the absence of breath sounds over the section of the lung which it supplies. With pulmonary tuberculosis the inspiratory sounds over the affected portion, e.g. over one apex, are often diminished or impure, and sometimes absent. With emphysema the breath sounds are diminished over both chests inasmuch as the respiratory alterations in volume of the persistently inflated lung are also diminished. The respiratory murmur is usually fainter over pleural effusions due to the fact that the fluid is a poor conductor of sound and tends, in addition, to press the lung away from the chest wall and more or less to immobilize it. Over massive pleural effusions the breath sounds are entirely absent. With extensive adhesions between the lung and chest wall the breath sounds are often diminished on account of the interference with proper inflation of the lungs.

In children the respiratory murmur is normally louder than in adults (**puerile breathing**).

If the patient, in an attempt to breathe loudly, produces loud noises in the pharynx, nose, or larynx, these noises are transmitted to, and may be heard over the lungs, most loudly over the upper and middle portions, i.e. in the fossæ supra-spinatæ, supra- and infra-claviculares, in the interscapular space and about the manubrium sterni. These adventitious noises may be avoided by directing the patient

to breathe as noiselessly as possible and at the same time to shape the lips as though to pronounce O or U. With pathological narrowing of the larynx, e.g. compression of the trachea by goitre, the resultant stridor may be transmitted so that it is audible over the lungs.

The term **increased breath sounds** is used to denote a change in the respiratory murmur, occurring during noiseless breathing, and characterized above all by a change in the sounds during expiration, i.e. the **expiratory phase** of the respiratory murmur is louder, longer and higher in pitch as compared with the normal vesicular respiration. Increase in duration and intensity of the expiratory sounds frequently is a sign of beginning or incomplete consolidation of the lung tissues. Limited to **one apex** such changes are often present early in pulmonary tuberculosis. It is, however, to be noted that **over the normal right pulmonary apex expiration is often of longer duration, higher in pitch and somewhat louder than over the left.**

When inspiration is divided into several short phases one speaks of "cog-wheel breathing." These interruptions in inspiration are usually synchronous with the heart beat, and are of little diagnostic value. (Cog-wheel breathing is commonly explained as due to rhythmic interruptions of the flow of air through a bronchus by the pulse wave in an artery pressing upon its wall. Ed.) The same may be said of the increase in intensity of respiration noticeable in the neighborhood of the heart with each systole (systolic vesicular breathing).

Bronchial Breathing (tubular breathing) has the quality of a high German "ch" and shows vibrations as rapid as 1000–2000 per sec. (See fig. 13.) These rapid vibrations determine the quality of bronchial breathing although less rapid vibrations are often demonstrable. Bronchial breathing is distinguished from vesicular not so much by its intensity as its quality. Under normal conditions true bronchial breathing is audible nowhere over the chest for the reason that the bronchi are surrounded on all sides by lung tissue so that the note produced in the bronchi is muffled or suppressed by the air-containing lung.

Under **pathological conditions** bronchial breathing is to

be observed wherever the lung is air-free, that is wherever the breath sounds produced in the bronchi are transmitted unhindered and unchanged to the chest wall. However, pure bronchial breath sounds are only to be heard over a relatively large area of consolidation which impinges upon a major bronchus. Bronchial breath sounds, audible over a given area, may be taken as **proof positive** that the underlying lung is **consolidated** and **air-free.** Bronchial breathing is present with all types of infiltration which lie immediately below or near the chest wall, e.g. with pneumonia and tuberculosis, also with **compression** of the lung above a pleural effusion, and in addition with **cavities** which lie near the chest wall and are surrounded by **air-free** tissue. If, on the other hand, an area of consolidation or a cavity lies deep in the lung surrounded by **air-containing** lung tissues, one hears over it not bronchial but vesicular breath sounds. The production of bronchial breathing in this case is not dependent upon the existence of the cavity but upon the consolidation of the lung tissue in its vicinity. Bronchial breathing is heard over consolidated lung only if the afferent bronchi are patent. If these bronchi are occluded by secretion or plugs of fibrin bronchial breath sounds are not heard; under these conditions the respiratory murmur is altogether lacking. It is for this reason that, in pneumonia, bronchial breathing may not be audible over the entire consolidated area but in certain areas the respiratory murmur is diminished or absent.

Over the larynx and trachea there is audible a respiratory murmur which is extraordinarily similar to the bronchial breath sound. This laryngeal or tracheal breathing is, however, not entirely identical with the pure bronchial breathing which is heard over massive pneumonic consolidation or over compressed, air-free lung. The tracheal breath sounds are somewhat lower in pitch (vibration frequency 600–800 per min.) and it may be demonstrated that they are complicated by the vesicular sound arising in the lung. Over the spinous processes of the seventh cervical and upper thoracic vertebræ, the adjacent portions of the interscapular space, and over the manubrium sterni, distant bronchial breath sounds may be heard, apparently obscured by the vesicular breathing (mixed breathing). If the stethoscope is placed successively against

the anterior aspect of the trachea, then on the side of the neck, and finally in the supra- and infra-clavicular fossæ, it becomes apparent that, with increasing distance, the higher tones of the tracheal breathing disappear first and that the broncho-vesicular breathing, with its increased expiratory phase, gradually passes over into vesicular breathing.

The respiratory murmur is designated as **broncho-vesicular** or of modified tubular quality when it can be distinguished as neither truly vesicular nor as bronchial. It is met with over early and incomplete consolidation of the lung tissues, i.e., wherever small areas of consolidation exist side by side with air-containing lung tissue; in short, when the conditions necessary for the production of both bronchial and vesicular breath sounds are present at the same time, so that both types are in reality audible at once. The respiratory murmur over pleural exudate must be described as broncho-vesicular when it is so faint that its character cannot accurately be described. With gradually advancing infiltration of the lung, e.g. in tuberculosis, the **expiratory murmur** is at first prolonged and higher in pitch while the inspiratory murmur remains unaltered or vesicular in quality. As the consolidation progresses the inspiratory phase of the breath sound becomes broncho-vesicular and the expiratory phase assumes the true bronchial quality. The inspiratory murmur is truly bronchial only when the lung is completely consolidated.

Both bronchial and broncho-vesicular breathing may be increased or diminished in intensity. Diminished bronchial breathing is heard over a pleural effusion when the underlying lung is consolidated, or compressed by the effusion.

The relation of the quality of the respiratory murmur (vesicular-broncho-vesicular-bronchial) to its intensity is indicated most clearly by the following table (page 50):

Amphoric breathing is the term applied to a deep, hollow, sighing respiratory murmur accompanied by high pitched ringing over-tones, which is heard over **large smooth-walled cavities** (of at least the size of a walnut), and occasionally over **pneumothorax.** It may be imitated by blowing across the mouth of a flask or bottle. It corresponds to the metallic ring elicited by percussion.

	Vesicular breath sounds	Broncho-vesicular breath sounds	Bronchial breath sounds
Increased	Vesicular increased in intensity (1)	Broncho-vesicular increased in intensity. (3)	Very loud bronchial (4)
Normal intensity	Normal vesicular	Normally loud broncho-vesicular	Medium loud bronchial
Diminished to absent	Distant vesicular (2)	Distant broncho-vesicular	Distant bronchial (5)

(1) puerile breathing.
(2) e.g. over pleural effusion with air-containing lung beneath.
(3) e.g. over early infiltration of the lung apex.
(4) e.g. over many tuberculous cavities.
(5) e.g. over pleural effusions with collapsed or consolidated lung beneath.

The breath sounds are described as **rough, or harsh,** when they no longer possess the relatively soft character of the normal vesicular breathing. Such changes represent a transition toward the production of râles and may sometimes be confused with them. Harsh breath sounds are heard in bronchitis and in the early stages of pulmonary tuberculosis at the lung apex.

Adventitious Respiratory Sounds

Râles. These are produced by the presence of fluid or tenacious material (mucus, pus, blood or transudates), in the air passages through which the stream of air bubbles in passing. The secretion causing the râles may often be identified by the examination of the sputum. The following types are to be differentiated:

Piping and whistling râles (rhonchi sonori and sibilantes), are **continuous** noises varying in quality from a high-pitched whistle to a deep hum. They are heard with inflammation of the bronchial mucous membrane, as a result of which tenacious secretion occupies the bronchial lumen but does not completely occlude it. These masses of mucus are set into vibration by the passage of the current of air. When râles are audible over the chest, clumps of mucus are often visible in the trachea upon laryngoscopic examination. These piping

and whistling sounds, often designated as "dry râles," are observed during expiration in bronchial catarrh and most commonly in bronchial asthma.

In contrast to these more or less continuous noises are the discontinuous, short, **crackling** sounds which are made by bubbles in the smaller bronchi. These arise when an obstructed bronchus is reopened during inspiration or when a bubble, formed in the bronchial secretion, bursts during respiration. These "bubbling râles" denote the presence of fluid (pus, mucus, blood, transudate) and are therefore designated as **moist râles.** If they are very numerous one may assume that large quantities of fluid are present in the air passages and that numerous bronchi are filled thereby.

"Bubbling râles" are further divided into coarse, medium and fine as they appear to arise in the larger bronchi and cavities or in the smaller bronchi. A particular type of fine râle is represented by the so-called "crepitant" râles. Such sounds are produced at the end of deep inspiration by the bubbling of air into alveoli which are filled with fluid or collapsed. Crepitant râles are heard only during inspiration and their presence is an important sign in the stages of engorgement and resolution of pneumonia, and in pulmonary œdema. In addition they are heard occasionally in the posterior and inferior portions of the lung during the first deep breaths (atelectatic râles), in patients or in healthy individuals who have lain for a long time in bed. Crackling râles may be imitated by stroking the hair over the ear or by the noise produced by an effervescing powder when first mixed with water.

Consonating râles. When bubbling râles are produced in the bronchi of an **air-containing** lung they sound indistinct and as though they arose in the depths of the lung. If, on the contrary, such adventitious sounds are produced in an **air-free, consolidated** portion of the lung they are higher pitched and more distinct, seem closer to the ear, and are designated as tinkling or, by the old term introduced by Skoda, **consonating.** Consonating râles are audible under the same circumstances as are bronchial breath sounds, i.e. over air-free lung tissue and over cavities surrounded by consolidated lung. Outspoken consonating râles may estab-

lish the diagnosis of consolidation even though the respiratory murmur be not typically bronchial, e.g. over small bronchopneumonic patches.

Râles having a **metallic quality** with very high overtones associated with a deep fundamental tone are encountered, together with metallic percussion note and amphoric breath sounds, **over large cavities,** or pneumothorax. Occasionally with pneumothorax one hears single metallic râles.

Râles may best be heard with deep respiration, immediately after coughing, and may be brought out by directing the patient to cough lightly from time to time.

Crackling and bubbling râles may sometimes be confused with the sound produced by swallowing or by movements of the shoulder blades. These latter sounds may be avoided by directing the patient to hold the shoulders back.

Pleural Friction Sounds

Such are heard whenever the pleural surfaces, which are normally smooth and moist, are roughened by a deposit of fibrin. The friction sound is produced by the rubbing of the visceral against the parietal pleura during respiration. It is an intermittent, creaking sound heard only during certain phases of respiration, and entirely absent when the patient holds his breath. As contrasted with other adventitious sounds, particularly with piping and sonorous râles, it is less continuous and is uninfluenced by coughing. Furthermore it is apparently superficial and seems to arise close to the ear. It is intensified by deep inspiration. Often a pleural friction is palpable through the chest wall. In the presence of pleural adhesions, as well as in the area occupied by a pleural effusion, the production of a pleural friction is impossible.

Voice Sounds

If one auscults over the chest of a healthy individual while he speaks one hears an indefinite murmur. The higher notes of the voice drop out so that only the deeper fundamental tones are audible. If the patient repeats the word "ninety-nine" in a loud voice the examiner hears only a muffled "nununun." If, on the other hand, one listens over air-free (consolidated or compressed) lung the voice of the

patient is heard loudly and distinctly, and the spoken word may sometimes be made out clearly, as though the patient spoke directly into the ear. The voice appears at the same time to be accompanied by a whispering noise and to be higher in pitch than at the mouth of the patient, since the lower tones of the voice are not transmitted. This phenomenon is known as **bronchophony or pectoriloquy.** (Such bronchophony, which is homologous with bronchial breathing, may best be recognized if the patient be directed to whisper loudly "one, two, three" while the examiner listens with the naked ear over the chest wall.) The presence of bronchophony makes it possible often to establish a diagnosis of pneumonic or tuberculous consolidation or of compression of the lung by pleural exudate, even though no outspoken bronchial breath sounds are to be heard. If the bronchi are occluded or if pneumothorax or a massive pleural effusion is present, the voice of the patient sounds muffled as heard at the chest wall.

A particular type of bronchophony, known as **ægophony,** is characterized by high-pitched, nasal, bleating voice sounds. This is encountered just below the upper border of a pleural exudate which has compressed the adjacent portion of the lung.

Vocal Fremitus

If one holds the palm of the hand* against his own chest wall while speaking loudly or singing, the chest wall may be felt to tremble. If, now, one sings the scale, it becomes apparent that this vibration is feeble or wanting during the high notes, begins about the middle of the small octave (somewhere about the f below middle c: 170 vibrations per sec.), and persists down through the lowest range of a bass voice. It has been shown that the vibration frequency of the vocal fremitus is exactly that of the sung or spoken tone. This phenomenon is probably to be explained as follows: The vibrations produced in the larynx are transmitted down the bronchi, so that the lungs and, with them, the chest wall are thus set in sympathetic vibration whenever the spoken tone corresponds with

*Since vibrations are more accurately perceived by bony than by soft tissues vocal fremitus may be more accurately estimated if the examiner presses the base of his palm or wrist against the chest wall of the patient.

Voice sounds
recorded from chest wall.

I. With *consolidation* (pneumonic infiltration) of one lung.

Over air-containing lung.

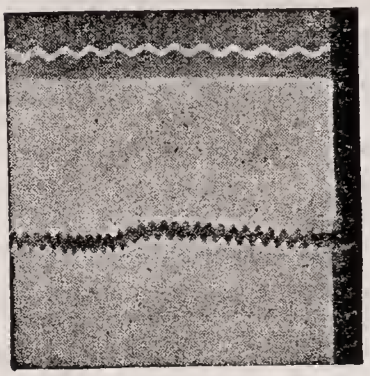


Fig. 14.

Over consolidated lung.

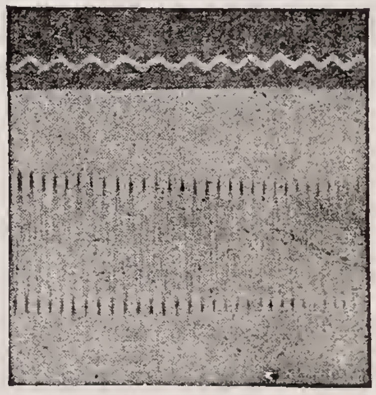


Fig. 15.

High voice (c# = 270 vibrations per sec.).

Fig. 16.

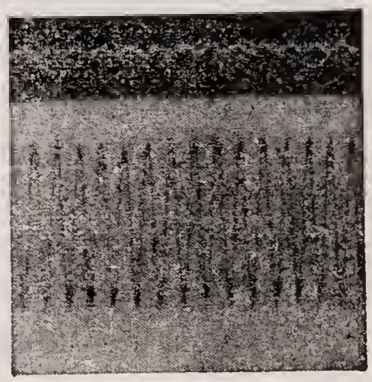


Fig. 17.

Low voice (b = 120 vibrations per sec.)

II. With pleural effusion.

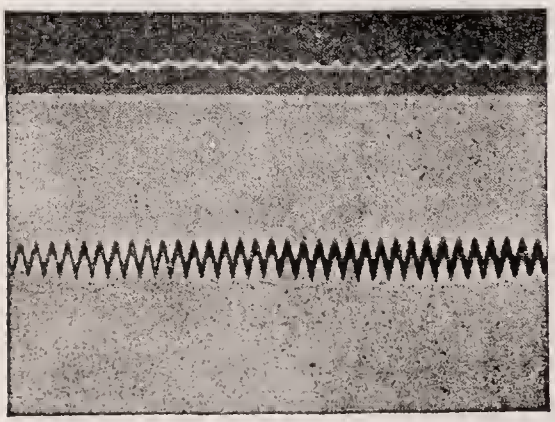


Fig. 18.—Normal side.

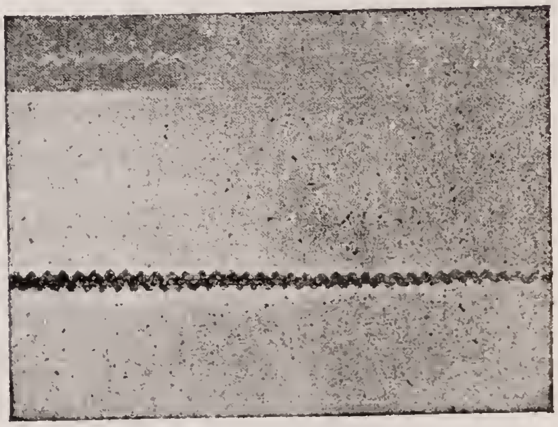


Fig. 19.—Side of effusion.

Moderately low voice (d = 145 vibrations per sec.).

their fundamental tones. The range of the female voice is usually higher (around 200 vibrations per sec.) than the fundamental tone of the lung; as a result in women, particularly among those with high voices, the vocal fremitus is scarcely palpable and therefore is of little diagnostic value. In children, on the other hand, the higher pitch of the voice corresponds to the fundamental tone of the smaller lung and fremitus is therefore easily palpable.

Vocal fremitus is tested by placing the hands simultaneously or one after another, upon symmetrical areas of the chest, and directing the patient to repeat in a loud, deep voice, the word "ninety-nine." It is **feeble** or **absent** over the area of dulness corresponding to pleural exudate or pneumothorax and this diminution of vocal fremitus is an important diagnostic sign of the presence of air or fluid in the pleural cavity.

Percussion	Tone	Vibrations per second	Auscultation
	c^5	4096	Metallic sounds
	c^4	2048	"ch" loudly spoken Bronchial breathing
	c^3	1024	
			Bronchovesicular breathing
	c^2	512	
High tympanitic note over abdomen.	c^1	256	
	b	241	
	a	217	
High note over partially consolidated lung.	g	191	
	f	170	
	e	161	Vesicular breathing
	d	145	
Normal lung note.	c	129	
	B	120	Maximum of vocal fremitus
	A	108	
	G	95	
Low note over emphysematous lung or pneumothorax.	F	85	
	E	80	
	D	72	
	C	64	
	C_1	32	
	C_2	16	

At the same time, the vocal fremitus may be intensified here and there over the area occupied by an effusion if pleural adhesions exist between the lung and the chest wall. This finding is often of importance in selecting a point for thoracentesis in attempting to aspirate an effusion. An **increase** in vocal fremitus particularly in that produced by the higher tones is met with over **consolidated portions of the lung,** i.e. in pneumonia, tuberculous infiltration and cavitation, (provided that the afferent bronchus is not plugged).

Over	Percussion note	Breath sounds	Râles	Voice sounds	Vocal fremitus
Air-containing lung	Loud, not tympanitic	Vesicular		Normal	Normal
Consolidated lung	Dull, sometimes tympanitic	Bronchial	Consonating (crackling)	Increased	Increased
Large cavities and pneumothorax	Tympanitic or metallic	Amphoric or absent (1)	Metallic consonating	Variable (1)	Variable (1)
Pleural effusions	Absolutely dull = flat	Diminished to absent	Absent	Diminished to absent	Diminished to absent

(1) Over a cavity the breath sounds, voice sounds and vocal fremitus are increased; over pneumothorax diminished to absent.

Succussion Splash

Succussio Hippocratis, i.e. a ringing, splashing noise, is heard when the patient is grasped by the shoulders and shaken, if both air and fluid are present in the pleural cavity (with sero- or pyo-pneumothorax). This sound may be imitated by shaking a large flask partly filled with water.

SPUTUM

The sputum is composed of the secretion of the mucous membrane of the trachea and bronchi. It may contain pus arising at any point in the respiratory apparatus, and also such of the secretions of the pharynx and sinuses as may be

thrown out into the mouth. Finally, in addition to the saliva and the secretion of the buccal mucous membranes, the sputum may sometimes contain particles of food.

According to their **preponderant constituents** sputa are to be classified as:

mucoid	serous
purulent	sanguinous

or as muco-purulent (with preponderantly mucoid characteristics) and purulo-mucoid (consisting mainly of pus) sanguino-mucoid, sanguino-serous, etc. Various types of sputa are further to be differentiated according to whether their constituents are **thoroughly mixed** and confluent, or are separated. If the former be the case it is apparent that the mucus-producing areas of the bronchus are the same as those from which the blood or pus arises. If the latter conditions obtain, the blood or pus has apparently accumulated in a circumscribed area, as, for example, in a cavity and has been covered with a sheet of mucus during its passage through the bronchus.

Pure mucoid sputa occur principally in the various forms of bronchitis. The sputa from the posterior nares, which are raised by clearing the throat, but not by coughing, consist usually of tenacious and often partly desiccated mucoid masses.

Purulent sputa appear following the rupture of an abscess of the lung, or of an adjacent organ, or the emptying of an empyema into a bronchus.

Homogeneous muco-purulent sputa occur in diffuse bronchitis. In diffuse chronic purulent bronchitis (bronchoblenorrhœa) the watery purulo-mucoid sputum separates into three layers in the sedimentation glass. In pulmonary tuberculosis the sputum is usually purulo-mucoid and homogeneous; pus is present in shreds or globules surrounded by a sheath of mucus. The sputum from very large cavities may sometimes be composed of several confluent globules.

Sputa made up of **pure blood** (hæmoptysis) occur in the event that, in some portion of the respiratory system, a blood vessel is eroded by ulceration, with the formation of a small aneurysm. Blood **coughed up** during an hæmoptysis is to be

differentiated from that which is **vomited** following a gastric hæmorrhage chiefly by the fact that it is bright red and foamy and has not undergone partial digestion. Hæmoptysis occurs most frequently in pulmonary tuberculosis and may appear at any stage of the disease; also in bronchiectasis, in the presence of foreign bodies in the bronchi, syphilis of the lung and pulmonary abscess, gunshot wounds of the lung, and finally with aneurysm of the aorta. Blood which arises in the nose or nasopharynx is expectorated without coughing or vomiting and is usually of a bright red color.

Serous, watery, very foamy sputa, similar to the beaten white of an egg, occur with pulmonary œdema.

Homogeneous sanguino-mucoid (yellowish or rusty) sputa occur in pneumonia, rarely with carcinoma or sarcoma of the lung. **Sanguino-serous** (prune juice) sputum occurs with pulmonary œdema, in the course of lobar pneumonia and with pulmonary infarction. This is not to be confused with the **blood-tinged saliva** (red-brown, thin and having a stale odor), which is raised by malingerers or hysterical individuals, and is produced by sucking the gums, or with the blood-tinged, fœtid, posterior nasal discharge of chronic tonsillitis and pharyngitis.

The **consistency** of the sputum is principally dependent upon its **content of mucus;** very mucoid sputa, as for example those of the asthmatic, or of some cases of pneumonia, are sometimes so tenacious that they will scarcely flow out of the glass.

The protein content of the sputum is usually low in all cases in which the sputum is a product of the increased secretion of the bronchial mucous membrane, as in asthma or bronchitis. If, on the other hand, with an inflammatory process (pneumonia) or with transudation (pulmonary œdema, chronic passive congestion of the lung in heart disease), there is poured out from the capillaries into the alveoli and bronchi a fluid of relatively high protein content, the sputum may show a considerable proportion of protein. Determination of protein content of the sputum may therefore assist in a differential diagnosis between these conditions.

To test the protein content of the sputum, place a not too small amount in a small glass vessel, add thereto approxi-

mately twice the volume of a 3% aqueous solution of acetic acid and shake vigorously. The mucin is thereby precipitated and the characteristic proteins remain in solution. Filter through paper and add to the filtrate a little potassium ferrocyanide solution. A heavy precipitate indicates a considerable amount of protein in the sputum, and is suggestive of an inflammatory or congestive process in the lung. A flocculent precipitate argues against the existence of a simple bronchitis or asthma.

Odor: Foul-smelling sputa occur with processes of decomposition, within the bronchi or lung (bronchitis fœtida, or gangrene of the lung).

Color: Aside from the yellow-green color caused by the presence of pus, the sputum may be red, brown, or brownish yellow due to the presence of blood pigments in various stages of decomposition. An **orange-color** indicates the presence of hæmatoidin in the sputum and occurs with lung abscess or sometimes due to the rupture of a liver abscess with an outpouring of bile pigments into the lung in cases of echinococcus cyst of the liver.

A **bright yellow** or **greenish-yellow** color in the sputum results from the action of bacteria, particularly if the specimen has remained for some time in the specimen cup. If one inoculates a second specimen from such sputum the same yellow tint may appear in it. A **greenish color** may indicate the presence of the green bile pigment, biliverdin, and is found in pneumonia with jaundice; in caseous pneumonia the sputum may sometimes be grass green in color. **Black sputa** occur in individuals who breathe an atmosphere containing coal dust or soot, i.e. in coal miners, iron workers and chimney-sweeps. In iron workers there may also occur from time to time orange-colored or red sputa. In bakers and millers who breathe flour dust one may sometimes encounter a **white paste-like** sputum which shows on microscopic examination small kernels of starch.

The **amount** of sputum may be very variable depending upon the associated disease; the greatest quantities are found in cases of bronchoblennorrhea, in extensive bronchiectasis and tuberculosis with cavitation and in pulmonary œdema, as well as with abscesses and empyemata which have ruptured into bronchi.

MORPHOLOGICAL CHARACTERISTICS

In the sputum of lobar pneumonia, of true bronchitis fibrinosa and diphtheria of the larynx and trachea, one sometimes finds **fibrinous casts** of portions of the bronchial tree. To isolate such a cast the sputum must be shaken with water. Such clots of fibrin are stained red with Ehrlich's triacid stain whereas the Curschmann spirals are stained green.

Curschmann spirals, strands of mucus drawn taut like a rope, and often containing a central fibre, are found principally in those chronic forms of bronchiolitis which tend to have frequent relapses, and which are often complicated by asthmatic attacks. On the other hand, Curschmann spirals may be entirely lacking in some patients with asthma, or may occur in individuals who have no such disease. These are almost always distinguishable macroscopically as fine fibres, and occur most frequently in small sago-like clumps of mucus; their true nature may, however, only be proven microscopically. Not infrequently in cases of asthma there occur delicate fibres in the form of spirals, of about the diameter of a red blood corpuscle (so-called isolated central fibres). Following the pseudo-asthmatic attacks which occur with severe dyspnœa, one sometimes finds in the sputum bronchial casts composed of inspissated mucus, which are not infrequently confused with the fibrin casts described above.

Strands of lung tissue are found in the sputum with extensive destruction in the lung, particularly lung gangrene, more rarely with lung abscess. They appear as dark brown flakes which may, however, be broken up only with difficulty, and which have usually a nauseating odor.

Echinococcus-hooks appear with hyatid disease of the lung or pleura or with the rupture of an echinococcus cyst of the liver into the lung.

MICROSCOPIC EXAMINATION OF THE SPUTUM

Leucocytes are always present in the sputum and in greater numbers the more purulent its character. The white blood cells are often in various stages of disintegration, with destruction of the nucleus, as for example, in bronchitis fœtida, pulmonary gangrene and with rupture of an empyema. Leucocytes containing fat-like, eosinophilic glob-

ules are to be found in great numbers in the sputum of bronchial asthma and in lesser numbers in that of chronic bronchitis and tuberculosis. For methods of staining (methylene blue-eosin) see the chapter on Blood. However, their presence is usually demonstrable without staining; the refractility and the size of their droplets are sufficiently characteristic of the eosinophilic leucocytes even in unstained preparations.

Red blood corpuscles are always present in blood-stained sputum; but sometimes they may be discovered by microscopic examination, after staining, in sputum which macroscopically does not appear to contain blood (e.g. in bronchopneumonia).

Cells or **fragments** of various types of **epithelium** are sometimes to be found in the sputum: **Pavement epithelium** from the mouth or lips, and **cylindrical** epithelium from the nose or nasopharynx, the larynx or particularly from the bronchi. Such cells appear in the sputum with any acute inflammation of these mucous membranes and are particularly abundant in bronchial asthma. The cells of the **alveolar epithelium** of the lung are large, round or ovoid, with the vesicular nuclei and cytoplasm containing particles of fat, carbon, or myelin. This myelin which may often appear in glistening droplets or biscuit-shaped masses, sometimes lying between the cells, is particularly abundant in chronic bronchitis. It occurs most frequently in the sago-like, tenacious masses of mucus in dry catarrh of the bronchi and in emphysema.

Heart-failure-cells are cells of the alveolar epithelium containing disintegrated blood pigment. They are present in chronic passive congestion of the lung, e.g. with the brown induration occurring with mitral disease, and, in addition, with hæmorrhagic infarction. If large numbers of heart-failure-cells are present in the sputum in clumps, they may often be recognized macroscopically as small brownish-yellow masses. If such sputum is mixed with hydrochloric acid and a 10% solution of potassium ferro-cyanide the iron-containing pigment of the heart-failure-cells is colored the deep blue of Prussian blue.

Fibres of elastic tissue occur in the sputum with any

sort of destructive disease in the respiratory passages, particularly with pulmonary tuberculosis and lung abscess. They appear as twisted, wavy, glistening threads. Their presence is positive evidence of the existence of destructive, ulcerative processes in the respiratory passages. In lung gangrene the elastic fibres are sometimes wanting, due to the presence of an autolytic ferment in the sputum.

Elastic fibres may usually be demonstrated by mixing a small portion of the sputum on a slide with a drop of 10% potassium hydroxide. Or a larger amount may be digested with an equal quantity of 10% potassium hydroxide upon the water-bath until the mixture is homogeneous; the sediment may then be examined microscopically after centrifugation or sedimentation. To stain the elastic fibres in such sediments, decant the supernatant fluid and add to the sediment several cc. of orcein solution (orcein 1.0, absolute alcohol 80.0, distilled water 40.0, concentrated HCl 2.0) and hydrochloric acid, drop by drop, until a faint red color appears. The mixture is then heated for several minutes over a boiling water-bath and decolorized with acid alcohol (concentrated HCl 1.0, alcohol 200.0, water 50.0). Centrifuge again and repeat the staining and decolorization of the sediment twice. The elastic fibres are thus stained a reddish violet and can easily be differentiated. Elastic fibres from food particles may sometimes lodge in the mouth, be expectorated, and lead to confusion.

Tumor cells occur with sarcoma or carcinoma of the respiratory passages and are sometimes only to be differentiated with certainty from the cells of the alveolar epithelium when the former appear in masses.

Fatty acid crystals, fine, bent, colorless needles, occur in putrid bronchitis, lung abscess and lung gangrene. Upon heating they melt, forming fat droplets. They are found most frequently in yellowish-white kernels the size of a head of a pin or larger, having a nauseating odor.

Hæmatoidin appears in the form of amorphous brownish-yellow granules, in rhomboid plates, or tufts of needles of the same color. It is present with old hæmorrhage in the lung or with rupture of an abscess of the lung or of an adjacent organ, e.g. the liver.

Charcot-Leyden crystals, sharp-pointed, colorless, glistening octahedra, are particularly abundant in bronchial asthma but sometimes occur with other diseases of the bronchi, or with rupture of echinococcus cysts into the bronchi. These are found with least difficulty in yellowish flakes and streaks of sputum.

Microörganisms are present in every sputum, relatively few in number in the pure mucoid sputum of chronic bronchitis, asthma and chronic passive congestion of the lung, somewhat more abundant in purulent expectorations (predominantly staphylococcus and streptococcus), and in large numbers in the sputa of various conditions involving putrefactive destruction of lung tissue. Of particular diagnostic significance are **tubercle bacilli.** To examine for tubercle bacilli select a purulent bit of sputum since such masses are more often expectorated from an ulcerated area. The procedure for staining the dried preparation of sputum is described in the chapter on microörganisms. In the rusty sputum of pneumonia, there are pneumococci in abundance appearing in the form of diplococci and often encapsulated. Since pneumococci in the stained preparation can sometimes be distinguished only with difficulty from other cocci, e.g., streptococci, culture or animal inoculation is sometimes necessary. White mice which have been inoculated intraperitoneally with material containing pneumococci die within twenty-four to forty-eight hours and show in the peritoneum great numbers of pneumococci. Occasionally there are present in the sputum filaments of **aspergillus** (pneumonomycosis aspergillina) which are best demonstrated in a preparation treated with 10% potassium hydroxide. In addition, with putrid bronchitis as well as in the expectorated plugs from the tonsils, there are sometimes found filaments of leptothrix which stain brown or blue with Gram's solution. Micrococcus tetragenus occurs in bronchitis and cavitation in the lungs. With these conditions and sometimes with bronchial carcinoma sarcinæ may appear. In actinomycosis of the lungs actinomyces are found in the sputa, (see chapter on Parasites and Infectious Diseases).

For the more exact bacteriological examination of the sputum and in particular for microörganisms which, like

the tubercle bacillus, cannot be demonstrated by simple staining, e.g., influenza bacilli, pneumococci, staphylococci, streptococci, etc., the method of R. Koch is particularly valuable. The sputum is collected in a sterile Petri dish. A mass of sputum is removed with a fine pincette and washed several times with sterile water or normal salt solution in order to remove from it the accumulated saliva with its innumerable bacteria. From the center of this mass of sputum a small portion is removed for staining or culture.

PHYSICAL SIGNS OF THE MORE IMPORTANT LUNG DISEASES

Lobar Pneumonia

Percussion note softer (duller), higher-pitched and shorter, sometimes slightly tympanitic, over the consolidated lung area. Upon auscultation in the stage of engorgement crepitant râles, in the stage of consolidation (hepatization) bronchial breath sounds, bronchophony and sometimes consonating râles, in the stage of resolution crepitant râles again; vocal fremitus increased. In the X-ray examination there appears in the area of pneumonic consolidation a shadow which begins for the most part centrally, near the lung hilus and spreads out during the next few days over the lung. The process of consolidation is only demonstrable by dulness and bronchial breathing when it has reached the surface of the lungs. See also chapter on Infectious Diseases. Sputum rusty or bloody and contains quantities of pneumococci or streptococci.

Pleuritis with Effusion

With a collection of fluid in one pleural cavity the affected side is visibly fuller and moves less with respiration. Over the exudate the percussion note is either flat or very dull and short, and the percussing finger feels a sense of increased resistance; suppression of breath sounds and of vocal fremitus. Above the effusion the percussion note over the compressed lung is often tympanitic; bronchial breath sounds, bronchophony and ægophony. The upper margin of a pleural exudate reaches its highest point in the posterior axillary line and

sinks toward the vertebral column and anterior costal margin. Upon change in position of the patient this upper margin undergoes little or no displacement. With massive effusion exerting positive pressure the heart and mediastinum are

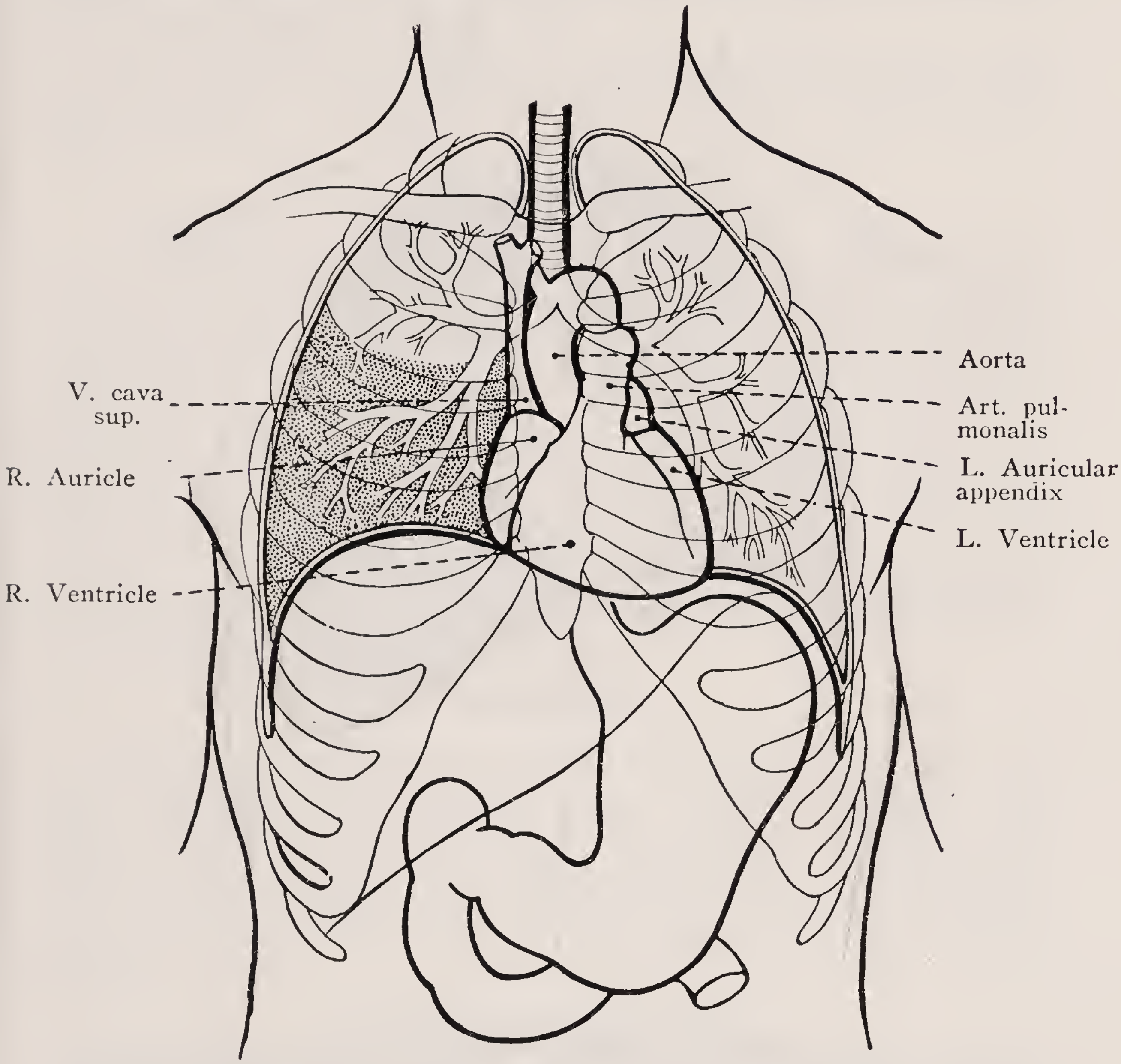


FIG. 20.—Schematic representation of pneumonia of right middle lobe; over the consolidated lung portion percussion dulness, bronchial breath and voice sounds and increased vocal fremitus are demonstrable. The figure may serve also to show certain topographical anatomical relationships.

displaced toward the opposite side, the diaphragm is depressed and the complementary space filled. With massive left-sided effusions the area of dulness may extend nearly to the costal margin. However, with a small effusion in the left pleural cavity, which exerts negative (less than atmospheric) pressure the lower limit of dulness extends only to the sixth rib leaving the normal, tympanitic note of the

stomach over Traube's semilunar space. Upon fluoroscopic examination a pleural effusion casts a dense shadow extending higher in the lateral portion of the chest than in the median. If a pleuritis heals after the resorption of the fluid adhesions

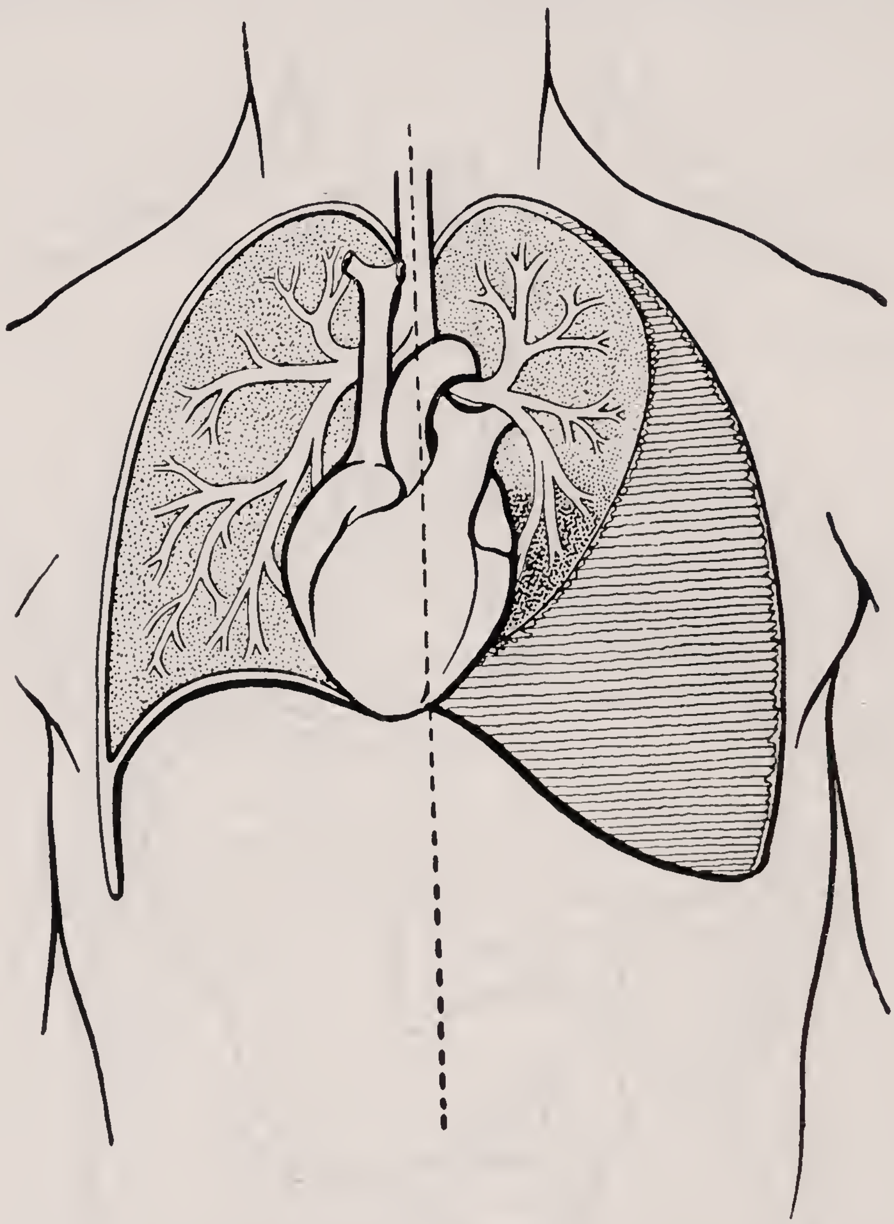


FIG. 21.—Diagram of a pleural effusion on left side with widening left half of thorax, compression and partial atelectasis of left lung. Deposit of fibrin upon left pulmonary and parietal pleura, displacement of heart toward right, depression of diaphragm and filling of left complementary space by fluid causing decrease in area of Traube's semilunar space. Over the effusion dulness to flatness, vocal fremitus absent, breath sounds absent or of distant bronchial quality. Above the effusion pleural friction rub. Cardiac dulness to the right.

may develop between the two pleural surfaces, and, with the shrinking of this new-formed connective tissue, the affected half of the thorax may be retracted and the adjacent organs drawn toward the side of the pleurisy.

(With pleural effusion there is, too, a triangular area of dulness next to the spine upon the sound side (paravertebral

triangle of Grocco). The apex of this triangle reaches the level of the effusion and the upper border falls steeply to the lower margin of the normal pulmonary resonance. This sign is sometimes of value in distinguishing pleural effusion from pneumonia or tumor. Ed.)

Dry pleurisy, i.e. deposit of fibrin upon the pleura without the effusion of fluid, is characterized by an audible pleural friction rub.

Emphysema

Barrel-shaped enlargement of the thorax. Depression of the lower lung borders; depression and diminution in size of the absolute cardiac dulness; suppression of breath sounds; often piping, whistling and bubbling râles as a result of the accompanying bronchitis. X-ray examination shows the thorax unusually wide, the lung areas strikingly translucent, the ribs coursing horizontally, the diaphragm flattened and low, the heart almost perpendicular. Abnormally low-pitched percussion note over the lungs. (Percussion note somewhat tympanitic in some cases. Ed.)

Bronchitis

Normal percussion note; vesicular breath sounds, sometimes suppressed in certain areas. Diffuse bubbling râles particularly over the lung bases posteriorly, or piping and whistling râles. With catarrhal inflammation involving only the trachea and the larger bronchi râles are often entirely lacking.

Pulmonary Tuberculosis

Tuberculous infiltration begins in the majority of cases at or near the apex and, even in the later stages, is generally more advanced in that portion of the lung. Tuberculous disease may, however, commence in the lower portions of the lung. In the early stages the percussion note is shorter and somewhat higher in pitch (less deep), later of a softer quality (dulness) over the affected portion of the lungs; the breath sounds bronchovesicular, often with suppressed or roughened inspiratory phase, and prolonged and somewhat intensified expiratory phase, and scattered crepitant râles. In the more advanced stage dulness increases and spreads, the breath

sounds become bronchial; consonating râles, and retraction of the supra- and infraclavicular fossæ on the affected side.

Cavities are only to be demonstrated with certainty if they are surrounded by consolidated tissue and lie near the

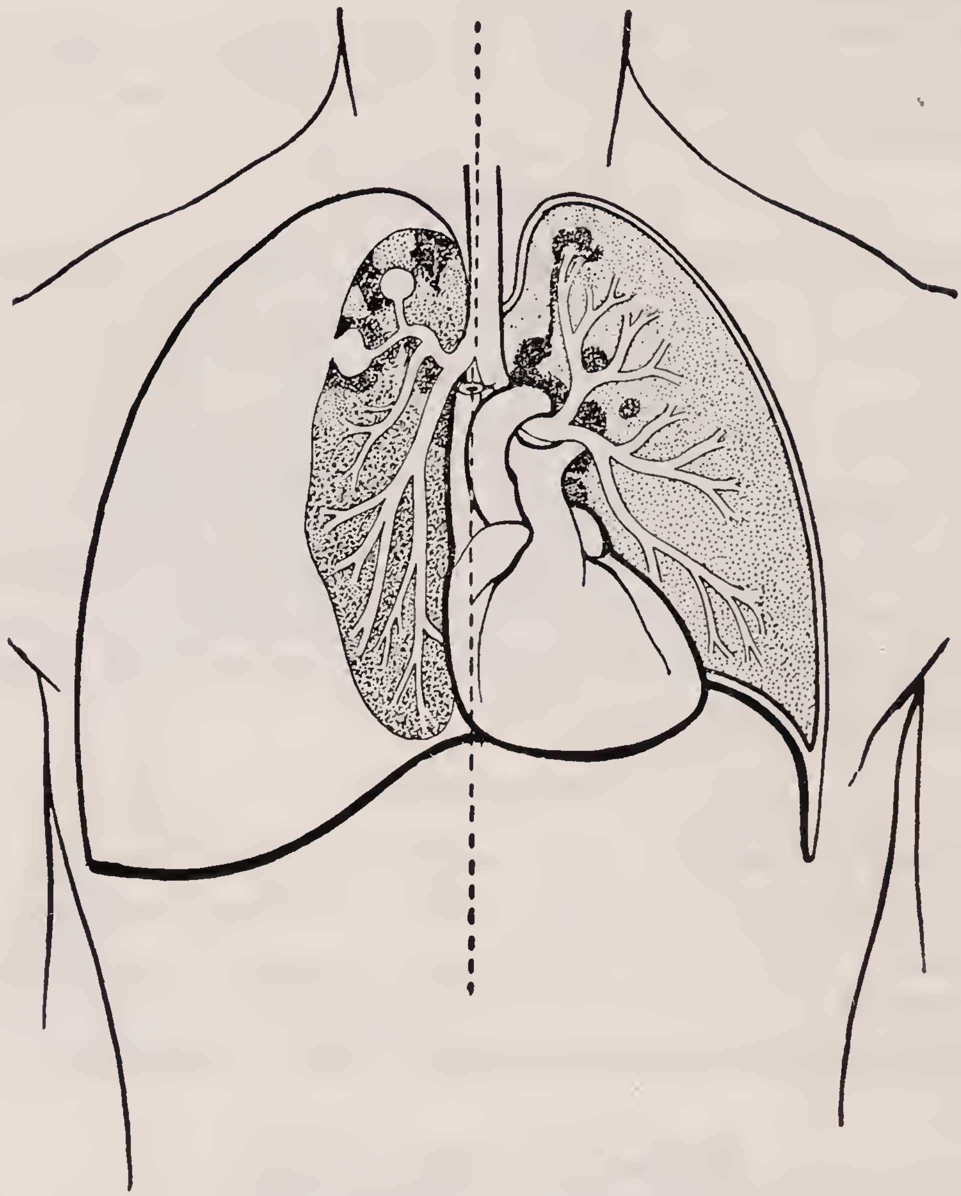


FIG. 22.—Diagram of a right-sided pneumothorax following rupture of a tuberculous cavity in the lung. Widening right half of thorax, collapse and atelectasis of the right lung. Massive accumulation of air in right pleural cavity with displacement of right diaphragm downward and of the heart toward the left. Over the pneumothorax percussion note abnormally loud and low-pitched, metallic ring with coin test, breath sounds absent or distant and amphoric, vocal fremitus diminished. In both apices are indicated tuberculous areas which would cause differences in percussion note over apices, suppressed or bronchovesicular breath sounds with accentuation of expiration. At the left apex a primary area of tuberculous infiltration with thickened lymphatics leading to enlarged and caseous glands at the hilus.

chest wall. They produce a high-pitched tympanitic percussion note which becomes louder and deeper as the cavity enlarges by destruction of the adjacent lung tissue. Occasionally there occurs Wintrich's or Gerhardt's change in pitch and the cracked-pot sound. Over such a cavity one hears

bronchial breath sounds and coarse bubbling râles. A large, smooth-walled cavity sometimes produces a metallic percussion note, amphoric breath sounds and metallic tinkling râles. Since the tympanitic note and the cracked-pot sounds, as well as changes in pitch, may occur with consolidation of the lung tissue in the absence of cavity formation, the metallic phenomena are the only pathognomonic signs of cavitation. Since these signs are often lacking the diagnosis of a cavity is frequently only to be conjectured.

By fluoroscopy or in the X-ray plate tuberculous infiltration is to be recognized by the presence of fleck-like shadows. Enlarged lymph glands at the hilus produce a round shadow. The diseased lung apex is often diffusely clouded, distinctly smaller, and clears less after coughing or deep respiration. Cavities are seen in the X-ray as clear areas surrounded by a dark wall and occasionally may show the presence of pus with a horizontal fluid level.

Pneumothorax

Enlargement and immobility of the affected side of the chest; abnormally loud and deep, although usually not tympanitic, percussion note extending above the normal lung border. Displacement of the adjacent organs (particularly heart and liver). Metallic ring or coin sound on percussion. Breath sounds diminished or absent, sometimes amphoric; diminished vocal fremitus. With the simultaneous presence of fluid, (i.e. with sero- and pyopneumothorax), immediate change in the fluid level on change of position of the patient from erect to horizontal; Succussio Hippocratis. Radioscopically a simple pneumothorax appears as an unusually translucent area in the affected half of the thorax, the lung as a shadow displaced against the hilus, and the displacement of the adjacent organs is apparent; with simultaneous effusion the horizontal fluid level is visible and the movement of its surface can be made out with changes in position and with respiration. With deep inspiration the diaphragm on the normal side may be seen to descend whereas on the side of the pneumothorax the fluid level is occasionally tossed upward (due to swinging motion of the diaphragm). Upon shaking the patient one sees the splashing of the exudate corresponding to the Succussio Hippocratis.

CHAPTER III

CIRCULATORY ORGANS

ANATOMY AND PHYSIOLOGY

THE heart rests upon the diaphragm. Its **right border,** formed by the right auricle, extends normally 3.5 to 4.5 cm. to the right of the median line or approximately a finger's breadth beyond the right sternal border. The **upper border,** made up of the great vessels, is found in the second intercostal

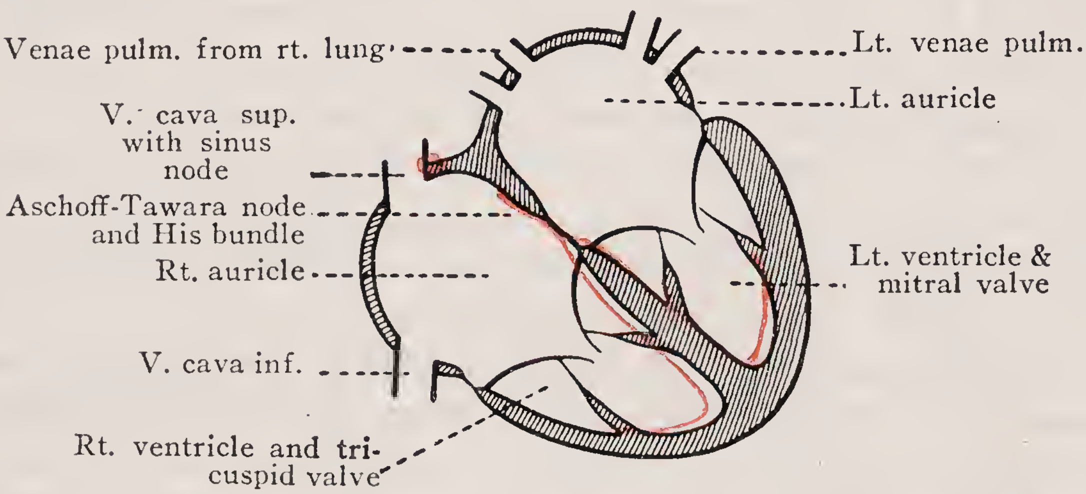


FIG. 23.—Diagram showing sinus node of Keith-Flack, Aschoff-Tawara node in auricular septum and the bundles of His from this node to the papillary muscles and the walls of both ventricles.

space or at the upper border of the third rib. The **left border** is that of the left ventricle and lies just outside the apex beat, in the fifth intercostal space just within the mammillary line, about 8–11 cm. to the left of the median line. The right auricle and ventricle are in contact with the anterior chest wall. The left auricle lies posteriorly toward the spine; the left ventricle occupies a posterior and inferior position, but its apex, the mitral orifice, the appendix of the left auricle lie close to the chest wall. The pulmonary valves lie beneath the left sternal border in the second intercostal space; the aortic valves are at the same level directly behind the sternum (cf. Figs. 20 and 23).

The heart reacts to its "inner stimulus" with rhythmic contractions. During each contraction, and for a short time thereafter, the heart muscle is unexcitable (refractory phase)

and following this the excitability gradually returns. At the point at which the vena cava superior enters the right auricle (sinus venosus) lies a node composed of a special type of muscle cells and containing many nerve cells (sinus node of Keith and Flack). This area apparently possesses the highest degree of irritability of the entire heart, and from it the normal excitatory process is transmitted to the auricles and from these to the ventricles. The impulse arising in this "sinus node" is transmitted to the auricles. Near the point of entrance near the coronary sinus, i.e., the opening of the coronary veins into the right auricle, and in the median wall of the right auricle lies another node of similar structure (Purkinje fibres and nerves), that of Aschoff and Tawara. This marks the origin of the bundle of His, which passes downward to the ventricular septum where it divides into a right and left branch and is distributed to the ventricular musculature. The excitatory process is transmitted from the node of Tawara through the His bundle from auricles to ventricles. The sinus node, the atrioventricular node (Aschoff-Tawara) and the His bundle, constitute together the **conduction system** of the heart. Through it the impulses arising in the sinus are normally transmitted throughout the entire heart, producing coördinate rhythmic contractions, the heart beat. The sinus node is, therefore, spoken of as the pace-maker of the heart. Under pathological conditions the auricles or ventricles may contract independently, due either to locally increased irritability in a particular portion of the heart, or to the introduction of an abnormal stimulus (extrasystoles). Independent contractions may also appear with disease of the conduction system, as the lower centers of the heart assume their inherent automaticity. Thus, for example, if there be a complete interruption of the His bundle the ventricles may beat with their own slow rhythm (about 30 beats per minute), independently of the more rapidly beating auricles.

Normally the excitatory process courses over the heart in an orderly fashion; it begins near the entrance of the great veins and spreads thence over the auricles. After a slight delay at the A-V node the excitation is distributed simultaneously to both ventricles; these contract together and

discharge their contents into the pulmonary artery and aorta.

With the beginning of ventricular systole the tricuspid and mitral valves close; the closure of these valves together with the contraction of the ventricles produces the **first sound.** The discharge of blood through the pulmonic and aortic orifices does not commence until the pressure in the

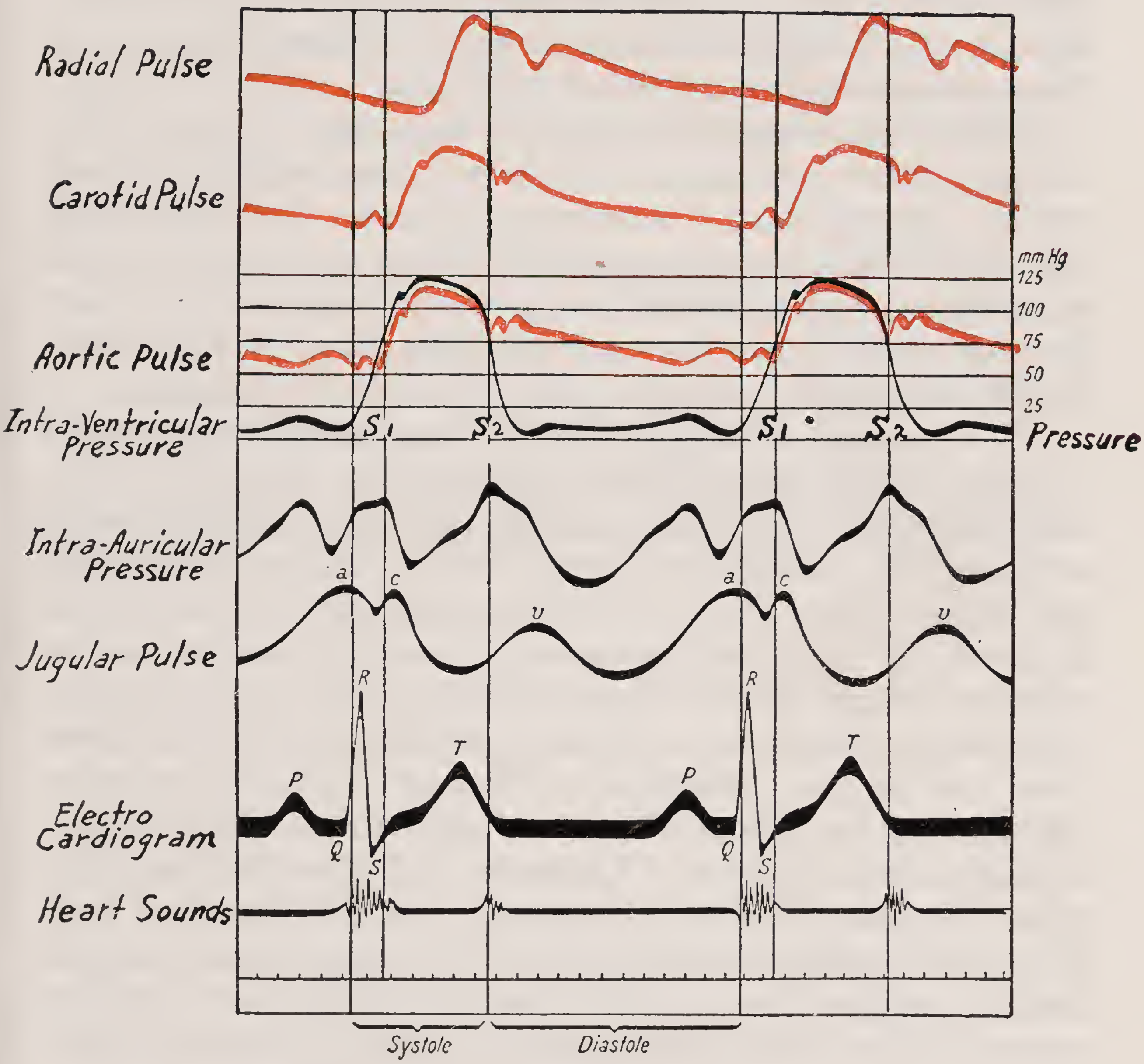


FIG. 24

ventricle has risen above that in the pulmonary artery and aorta. This first portion of systole, during which all valves are closed, is known as the **isometric period.** Ventricular contraction follows that of the auricle after an interval of .10–.15 of a second. After the ventricular contents have been discharged **diastole** begins; at this instant the pulmonic and aortic valves close producing the **second sound.** The duration of systole is

therefore marked by the interval between the first and second sounds and diastole by that between the second sound and the succeeding first sound. In Fig. 24 the time relations of these various phenomena are indicated. The delay in the carotid pulse as compared to the beginning of ventricular systole is caused not only by the isometric period of the ventricle (about .05–.07 seconds), but also by the interval required for the pulse wave to travel from the base of the aorta into the carotid (.02–.03 seconds). The transmission of the pulse wave in the arteries requires a further .05–.06 seconds.

With each contraction during rest each ventricle discharges about 70–100 c.c. blood, but does not empty completely. During sleep this output per beat is less; this is also the case in certain forms of heart disease and in many cases of excessive hypertension. A substantial increase in the output per beat of the left ventricle is also observed with aortic insufficiency and in many cases of Basedow's disease.

The "minute volume-output" of the heart is that amount of blood which passes in one minute from the right to the left ventricle. The cardiac output per beat is calculated by dividing the "minute-volume" by the number of systoles per minute. The minute-volume can be determined by the method of Fick, in which the oxygen content and the carbon dioxide content of the venous blood from the right heart are compared with those of the arterial blood, and at the same time the oxygen absorption and carbon dioxide excretion through the lungs are determined. In human beings a more suitable method is that of Grollman and Marshall,* in which a gas-mixture of known acetylene content is breathed from a bag, and, after a definite time, the absorption of this gas and of oxygen through the lungs is determined. By this method it has been shown that in human beings the minute circulatory volume at rest amounts to between 3.6 and 5.8 (average of 4.7) liters; after exercise it increases greatly and can rise to 9 or even 12 liters.

The contractions of the heart are automatic but are influenced by the **nervous system** as regards their strength and frequency; stimulation of the sympathetic (N. accelerator) brings about acceleration and augmentation of the beat

*Am. J. Physiol., 1928, **86**, 110.

whereas an increase in vagus tone, on the other hand, causes a slower rate and somewhat weaker contractions. The heart is also connected by efferent fibres to the medulla; this "N. depressor," incorporated in the human being in the vagus, is stimulated by rise of pressure in the aorta and through its connections in the medulla brings about a fall in blood pressure and a slowing of the cardiac rate.

Any increased circulatory demand is met by the heart under **physiological** conditions by an increased rate and increased diastolic filling. This is brought about by increased filling from the great veins, e.g. with exercise. The increased diastolic filling brings about greater initial tension of the ventricular musculature and this in turn leads to a greater strength of contraction. Under **pathological** conditions insufficiency of a valve may also lead to increased diastolic filling of the ventricle. Up to a certain point compensation is effected by dilatation; beyond this point excessive dilatation and myocardial insufficiency result.

An excessive load on the heart leads, after a time, to **hypertrophy** of the ventricular musculature; this takes place, however, only after several weeks or months. Such hypertrophy occurs in the presence of an abnormally high blood pressure; under these circumstances the heart is forced to empty against an increased resistance (hypertension). It may also follow certain valvular lesions in the face of which the output per beat is increased or impeded.

Dilatation of the ventricles, often associated with cardiac enlargement, results if abnormally large amounts of blood enter the ventricle during diastole as is the case with many valvular lesions and particularly in aortic insufficiency. Dilatation also occurs if the myocardium be functionally or organically impaired so that it cannot discharge the ventricular contents with systole; this is particularly the case in the presence of myocardial disease. A dilated heart may gradually hypertrophy or an hypertrophied heart may dilate if the myocardium becomes unable to bear its load. Dilated ventricles may sometimes contract asynchronously.

If the heart is no longer able to overcome the circulatory resistance and to furnish an adequate systolic output one speaks of myocardial insufficiency. The inevitable result is

stasis in that portion of the circulation afferent to the insufficient ventricle, i.e. with left heart failure in the pulmonary circulation and with right heart failure in the systemic veins and particularly in the liver. The circulatory rate is conspicuously slowed in myocardial insufficiency.

INSPECTION AND PALPATION

The **apex impulse** is that point farthest to the left of the mid-sternal line at which the cardiac impulse is **palpable** (it may or may not correspond to the point at which the heart beat is **most forceful**—i.e. the **point of maximum impulse).** In the normal adult the apex impulse lies in the 5th left intercostal space between the parasternal and mammillary lines. The circumscribed pulsation to which this term is applied is not due to the systolic thrust of the apex against the chest wall but rather to that of a portion of the **left ventricle. The apex impulse is displaced upward** with any elevation of the diaphragm, e.g. with meteorism, abdominal tumors, ascites, and during pregnancy. It is correspondingly **lowered** when the diaphragm is for any reason depressed.

Displacement of the apex impulse and cardiac dulness to the right occurs with left-sided pleural effusion or pneumothorax, or with shrinking of the right lung. Displacement **to the left** takes place with hypertrophy or dilatation of the heart, with right-sided pleural effusion or pneumothorax or with retraction of the left lung. When the apex impulse is conspicuously displaced to the left, e.g. with enlargement of the left ventricle, it comes, on account of the oblique course of the ribs, to lie in the 6th or 7th intercostal space.

The apex impulse may vary in intensity; it may be weaker than the normal, or more forceful (slapping, thrusting or heaving); it may sometimes be absent. The fact that the apex impulse is not palpable is no certain evidence of disease. While this may be true if the heart beat lack the normal force or may be due to an accumulation of fluid within the pericardium, the apex impulse may also be absent in the normal individual (with a thick chest wall, in obese individuals, or if lung be interposed between heart and chest wall).

A **forceful apex impulse** occurs with almost any increase in the activity of the heart, in fever, emotional excitement, cardiac neuroses, hyperthyroidism, after exercise, or drinking

strong coffee. Under these circumstances it is **tapping,** i.e. the pressure against the chest wall lasts only for an instant. A polygraphic record of the apex beat shows, in such cases, a steep ascending limb and a rapid fall. With **hypertrophy** of the left ventricle the apex impulse is **increased in force and heaving,** due to the fact that the intercostal spaces, and sometimes even the ribs, are pressed outward by the force of systole. With hypertrophy of the left ventricle the apex impulse is displaced to the left (often in the 6th intercostal space), its forceful pulsation is present over only a circumscribed area and at the point at which the apex of the heart (formed by the hypertrophied left ventricle) lies against the chest wall. It is characteristic of **right ventricular hypertrophy** that the most forceful pulsation is not localized at the apex of the heart, but is diffuse over that portion of the præcordium overlying the right ventricle. The pulsation may be particularly apparent over the 3rd left interspace at the sternal margin in the region of the conus arteriosus, or, with a short sternum or low heart, may be visible in the epigastrium. The heaving impulse of the hypertrophied right ventricle may be clearly felt by pressing the hand over the præcordium at the left sternal margin. Such an impulse over left or right ventricle is to be regarded less as a sign of hypertrophy of the heart wall than as an indication that the emptying of the ventricle is impeded. Increase in the force of the apex impulse is therefore not always evidence of increased functional capacity on the part of the heart muscle; it may occur with insufficient function, e.g. with myocardial insufficiency following valvular or myocardial disease.

The area occupied by the **visible cardiac impulse** may be extensive when the heart's action is particularly forceful or when a larger portion of the ventricle lies against the chest wall (e.g. with retraction of the left lung). The **chest wall may actually bulge forward** in the præcordial region with conspicuous hypertrophy and dilatation of the heart, particularly so if this has taken place early in life (e.g. with certain valvular diseases).

A **systolic retraction at the apex** is observed in the presence of adhesions between the heart, pericardium and chest wall. Under these conditions retraction is not limited to the apex but takes place over a wide area, and not only the intercostal

spaces but also the ribs are forcibly retracted with systole. Such a diffuse systolic retraction is not to be confused with one occurring in the neighborhood of the apex while the apex impulse itself may thrust outward with systole. This is produced by the diminution in size and change in position of the ventricle with systole and is of no pathological significance.

Pulsation in the epigastrium occurs with hypertrophy of the right ventricle, with an abnormally short sternum or with depression of the diaphragm.

With **dilatation (aneurysm) of the ascending aorta** there appears a pulsation in the second right intercostal space

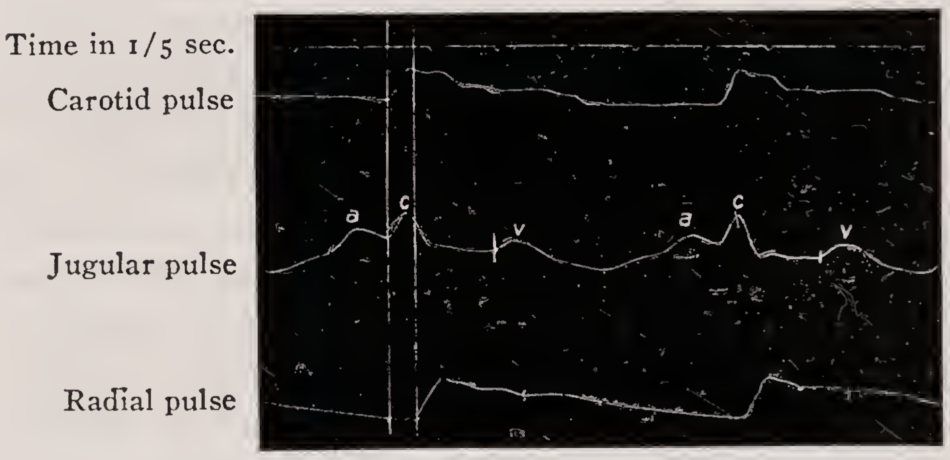


Fig. 25—Simultaneous record of carotid, jugular and radial pulses in a normal man.

near the sternal margin. The vigorous pulsation of the aortic arch may be palpable in the jugular groove with aneurysm of the aorta or with dilatation and lengthening of this vessel associated with aortic insufficiency. A palpable shock over the pulmonic area, corresponding to the closure of the pulmonic valve, is to be regarded as pathological only when associated with stasis in the lesser circulation; it corresponds to an increase in the intensity of the second pulmonic sound.

A **tracheal tug** is palpable in the presence of aneurysm of the aortic arch. When the cricoid cartilages are grasped between the tips of the fingers and the larynx lifted slightly upward or pushed to one side there is a rhythmic downward tugging of the trachea synchronous with systole.

The pulsations in the jugular bulb and in the vein above it furnish important information concerning the events in the right auricle. Such pulsations may be visible and their

relation to the carotid pulse may be made out by placing the finger upon the carotid in the neck.

The details of the jugular pulse are best studied in a graphic record obtained with a polygraph. Several component waves are distinguishable. The first is a presystolic auricular wave dependent upon the contraction of the auricle; it is designated by the letter A. Shortly thereafter occurs a systolic spike (the C wave) which is almost synchronous with the carotid pulse and is due to the shock of the closure of the tricuspid valve and the systolic impulse from the ventricle. Finally there occurs a wave (V) which is dependent upon the filling of the auricles at the beginning of diastole and corresponds to the time at which the tricuspid and mitral valves open and the blood begins to flow from the auricles into the ventricles. With pronounced venous stasis, and particularly with tricuspid insufficiency, there appears on the plateau between the C and V waves a so-called "congestion wave" giving rise to the "systolic venous pulse." By comparing records simultaneously obtained from the jugular and carotid pulse it is possible to analyze the various events taking place in the auricle and ventricle during the cardiac cycle, and to distinguish various types of arryhthmias (see Fig. 25).

Venous congestion and **cyanosis** occur with failure of the right heart, with valvular disease, or with obstruction in the lesser circulation. (Cyanosis is visible whenever the blood contains 5 gm. or more of reduced hæmoglobin per 100 c.c. Ed.)

Capillary pulse, alternate reddening and blanching demonstrable by pressing a glass slide against the forehead, or sometimes visible in the finger nails, is often observed with aortic insufficiency. (It is due to relaxation of the peripheral vascular field so that the pulse wave penetrates into the venous limbs of the capillaries. It appears with any condition associated with such vascular relaxation, e.g. fever or hyperthyroidism, or may be produced locally in the normal individual by placing the hand in hot water. Ed.)

PERCUSSION OF THE HEART

In outlining the **relative cardiac dulness** by percussion one determines first the position of the lower lung border in the right mammillary line and thereby the position of the

diaphragm; upon this the cardiac dulness is built up. By percussing in each interspace from without inward, determining the point at which the resonant note of the lung becomes duller due to the underlying heart or great vessels, the right and left borders of the cardiac and supracardiac dulness may be outlined.

In the normal individual the heart is, to a great extent, overlain by the free borders of the right and left lung. Only a small portion of the ventricle is in immediate contact with the anterior chest wall. By very light percussion it is possible to outline the lung borders and thereby to establish the area of the heart which is in contact with the chest wall, the **absolute cardiac dulness.** The percussion note in this region is not always absolutely flat in the usual sense of the word, i.e. not the same as that over the muscles of the leg. It may have a tympanitic quality when the stomach is filled with air. With pathological enlargement and hypertrophy of the heart the area of absolute cardiac dulness is usually increased in size and the note here often becomes more distinctly flat. In the healthy adult the upper border of the absolute cardiac dulness coincides with the lower border of the fourth left rib. Its right border courses along the left sternal margin, and its outer limit forms a gradual curve from the 4th costal cartilage to the apex; in many cases it does not extend to the apex but lies one or two finger breadths medial thereto. The lower margin of the cardiac dulness can be made out by percussion only when it extends downward and borders upon the tympanitic note of the stomach and intestines. Under normal conditions this is not possible since the cardiac dulness passes over directly into the dulness of the liver. In children the absolute cardiac dulness is relatively increased in size, in elderly individuals it is often smaller. With deep inspiration the area of absolute cardiac dulness is diminished due to the descent of the left lung border between the heart and anterior chest wall. This diminution in size fails to take place when the left lung is bound to the chest wall and pericardium by pleural adhesions, (adhesive mediastinitis). Since not only the size of the heart but the relation of the lung borders to it influence the size of this area it is not possible to say from the absolute cardiac dulness alone

whether the heart is normal or enlarged. With pulmonary emphysema, for example, the absolute cardiac dulness may be conspicuously diminished in size whereas the heart may be enlarged.

The actual size of the heart may only be determined by the percussion of the **relative cardiac dulness.** The right border extends from 3–4.5 cm. to the right of the median line but may lie at, or slightly within, the right sternal border; it may occasionally coincide with the right border of the absolute cardiac dulness at the left sternal margin. This latter condition obtains particularly in elderly individuals with rigid costochondral junctions or when the right auricle is covered by a layer of lung 4–5 cm. in thickness. The left border of the relative cardiac dulness lies just outside the apex impulse (8–11 cm. to the left of the median line). If the thoracic cage be narrow or the heart enlarged the outer border of the relative cardiac dulness may lie on the lateral portion of the chest wall. Percussion of the relative cardiac dulness is facilitated by directing the patient to breathe out as strongly as possible; by this procedure the lung borders are drawn back from over the heart. In children and young individuals in whom the chest wall is elastic the size of the heart may be accurately projected upon the chest wall by percussion. With a rigid thorax, on the other hand, and particularly with a low diaphragm or with pulmonary emphysema the relative cardiac dulness may be smaller than the actual size of the heart would indicate. If the relative cardiac dulness be unusually small it is not safe to conclude that the heart itself is smaller than normal, since, in certain conditions, particularly with emphysema, cardiac enlargement may exist in the presence of a cardiac dulness of normal size. If, on the other hand, the relative cardiac dulness exceeds the limits of the normal either to right or left it may safely be assumed that the heart itself is enlarged. The size of the cardiac dulness should be expressed in centimeters to right and left of the mid-line and not simply in relation to the sternal border or to the parasternal and mammillary lines.

The size of the heart, and therewith the borders of the relative cardiac dulness, vary in the normal individual within

certain limits. The size of the heart varies with increasing height and weight. Thus in young men of medium or light weight the right border usually lies from 3–4 cm. from the median line, in obese individuals it may extend 4–4.5 cm. The left border in small individuals extends from 8–9, and in larger men from 9–10 at most 11 cm. to the left of the median line. In women the relative cardiac dulness is smaller than that in men by ½ to 1 cm. in either direction; in individuals under 20 it is somewhat smaller, and in those over 40 slightly larger. Moreover, the position of the heart, and at the same time the magnitude of the relative cardiac dul-

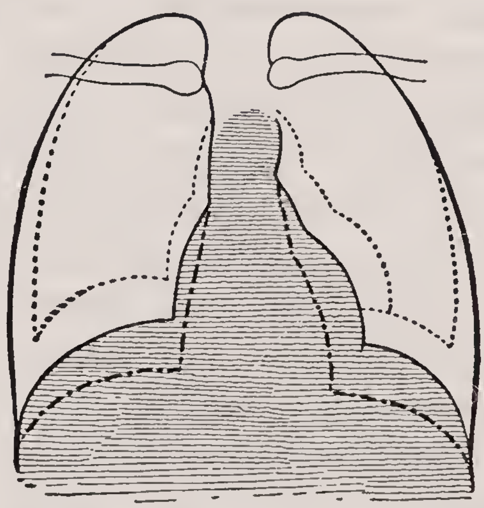


Fig. 26.—Diagram of cardiac shadow by fluoroscopy, position with normal inspiration (shaded area); at end of maximal expiration and with elevation of diaphragm (dotted line); with depression of diaphragm (broken line).

ness, is dependent upon the position of the diaphragm. With a low diaphragm and at the end of a deep inspiration the heart sinks downward, tends to be more perpendicular, and the diameter of the cardiac dulness is correspondingly reduced; with elevation of the diaphragm the heart lies more horizontally and the relative cardiac dulness is not only displaced somewhat upward but also increased in size to the left. Such an elevation of the diaphragm occurs in obese individuals with large amounts of abdominal fat, with ascites or tumors in the abdomen, and finally with pregnancy.

The relative value of light or heavy percussion in outlining the absolute cardiac dulness is dependent upon the individual; accurate results may often be obtained with

either method. The same is true of the determination of the relative cardiac dulness which may often be outlined as accurately with light as with heavy percussion.

Enlargement of the relative cardiac dulness is brought about by: Enlargement of the heart and particularly with cardiac dilatation; with hypertrophy of the heart muscle only if this be associated with dilatation of the ventricle.

Enlargement of the **left** ventricle produces an increase in size of the cardiac dulness almost exclusively to the left and not upward. With enlargement of the **right** ventricle the cardiac dulness is enlarged upward on the left side, often as far as the second rib, and may also extend abnormally far to the right. A considerable enlargement of the cardiac dulness to the right, particularly if this be associated with absolute dulness to the right of the right sternal margin, is indicative of enlargement (dilatation) of the right **auricle** or of pericardial effusion.

Hypertrophy of the **left** ventricle occurs with aortic stenosis or insufficiency, with mitral insufficiency, with long-standing elevation of blood pressure (hypertension) and the associated arteriolarsclerosis and nephritis, most conspicuously with the so-called contracted kidneys and finally with continued violent exercise (athletics).

Hypertrophy of the **right** ventricle takes place with congestion or obstruction in the pulmonary circulation: Mitral insufficiency and stenosis, pulmonic insufficiency, and tricuspid insufficiency.

Enlargement of the cardiac dulness occurs further with:

Effusion into the pericardium (exudative pericarditis). With this condition the cardiac dulness is conspicuously increased in all directions and tends to assume the form of an equilateral triangle with the apex in the first or second intercostal space, the right border extending to the right parasternal line (or even beyond) and the left border reaching outside the apex impulse.

Enlargement of the absolute cardiac dulness may occur without demonstrable enlargement of the heart, (i.e. with retraction of the left lung so that a larger area of the ventricle comes in actual contact with the chest wall), with mediastinal tumors or elevation of the diaphragm which bring

the heart into a more horizontal position. With pregnancy, ascites and abdominal tumors the cardiac dulness is not only displaced upward but also widened.

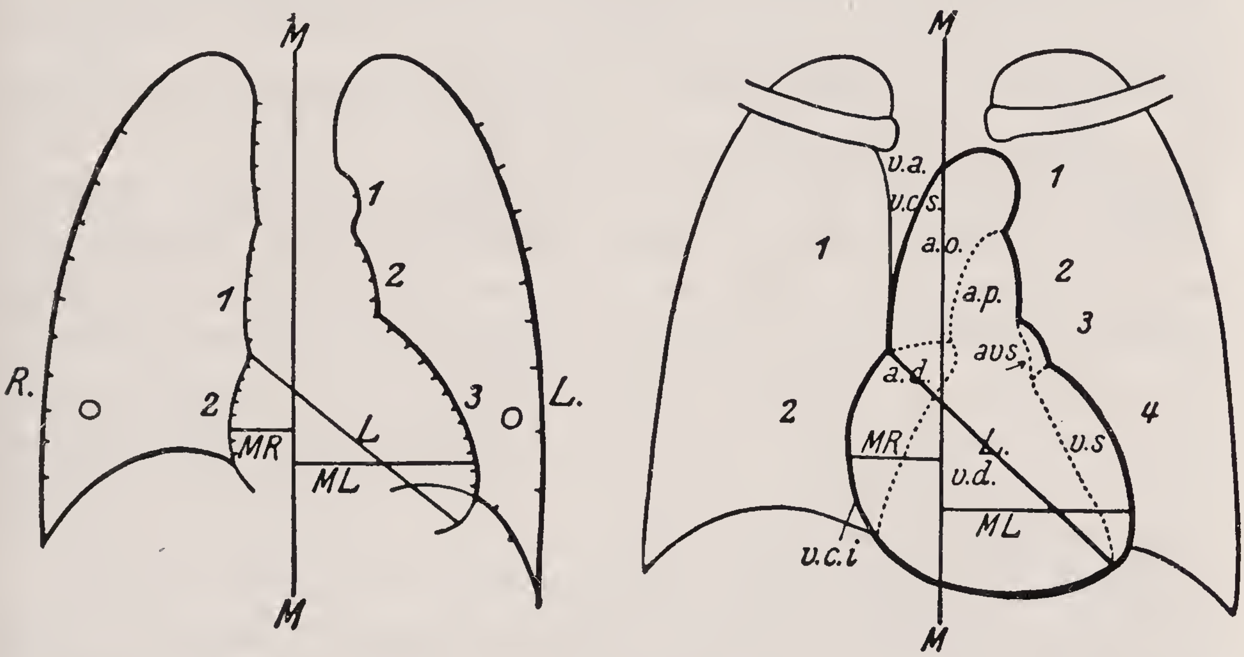
Decrease in size of the cardiac dulness is no sign of decrease in size of the heart but occurs most often with a low diaphragm and a correspondingly vertical position of the heart and a long thorax. In such cases the cardiac dulness extends well downward and is strikingly narrow ("dropped heart," see fig. 26). The relative cardiac dulness may also undergo an apparent decrease in size when, with increase in the sterno-vertebral diameter of the thorax, the heart lies well below the chest wall and is covered with the air-containing borders of the lungs.

Aneurysm of the ascending aorta may bring about a visible pulsation and impairment of percussion in the second or third right interspace at the sternal margin. Aneurysm of the arch of the aorta or of the pulmonic artery may produce similar signs in a corresponding area just to the left of the sternum. Dulness over the manubrium sterni may, in addition to changes in the aorta, be caused by mediastinal tumors, substernal goiter, enlarged thymus, and occasionally by stasis in the great veins. The great diagnostic significance of these percussion findings renders it advisable always to percuss the upper median portion of the thorax with the greatest care.

EXAMINATION OF THE HEART WITH THE X-RAY

This is carried out with the tube behind the patient at the exact level of the heart and the fluorescent screen or photographic plate against the anterior chest wall. Between the light areas occupied by the lungs there is visualized the **heart shadow,** continuous with the shadow of the great vessels and that of the vertebral column behind them. Within the shadow of the great vessels there is distinguishable, at the level of the second rib, a slight prominence corresponding to the aortic arch. Somewhat below it, at about the third rib, a second, somewhat less pronounced, curve is produced by the pulmonary artery and left auricle. The upper border of the left ventricle makes, with this curved line, an obtuse angle, and continues downward to the apex of the heart. The apex and the lower border of the cardiac shadow (formed by the right

ventricle) are obscured by the shadows of the diaphragm and liver. This is due to the fact that the apex of the heart and right ventricle lie, not upon the dome of the diaphragm, but in the scaphoid space between the anterior surface of the diaphragm and the chest wall. The right border of the cardiac shadow forms a curved line which corresponds to the outer surface of the right auricle and forms an obtuse angle with the



FIGS. 27 and 28.—Orthodiagram of heart with chambers indicated in dotted line.

Right border.

1st curve: v. a. Vena anonyma dextra.
v. c. s. Vena cava superior.
ao. Aorta ascendens.
2nd curve: a. d. Atrium dextrum.
v. c. i. Vena cava inferior with vena hepatica dextra.

Left Border.

1st curve: ao. Aorta.
a. p. Arteria pulmonalis.
au. s. Auricula sinistra (lt. auricular appendix).
v. s. Ventriculus sinistra.

Diameters

L. Long diameter.
MR. Median-right diameter
ML. Median-left diameter.
MR + ML. Transverse diameter.

right margin of the shadow of the great vessels (vena cava superior).

This method of examination is of invaluable assistance in demonstrating abnormalities of the heart (enlargement displacement) and of the vessels (aneurysm of the aorta), as well as the presence of tumors (substernal goiter, mediastinal masses, etc.). No accurate measurement of the heart may, however, be obtained in this way since the rays diverge from the target of the X-ray tube and, depending upon the distance of the heart from the target on one hand, and from the

screen on the other, the heart shadow is more or less exaggerated in size.

Far more exact measurements are to be obtained by **orthodiagraphy** (Moritz) in which all the rays from the tube are eliminated excepting those vertical to the screen. The patient lies upon or stands against the frame; behind him the tube is fixed in a movable carriage. Fastened to the carriage by arms which reach around in front of the patient is a visualizing apparatus so placed that it is always vertical to the tube. By moving this apparatus (and with it the tube) over the thorax of the patient the borders of the heart may be outlined upon transparent paper placed over the fluorescent screen. There is obtained in this manner a silhouette of the heart as projected by parallel rays against a horizontal plane. For purposes of orientation the mid-line of the sternum and the mammillary lines may be marked with lead paste so that they cast a shadow on the screen. This silhouette is then measured in centimeters. It is customary to record the greatest distances of the right and left borders of the heart from the mid-line (MR, ML, Figs. 27 and 28), and the length of the cardiac shadow corresponding to a line drawn from the border of the right auricle to the apex.

A somewhat less accurate record of the heart shadow may be obtained by the telcrœntgenogram (A. Koehler). The patient stands with the chest against the photographic plate which is enclosed in a cassette. The X-ray tube is then placed behind him at a distance of 2 meters and at the height of the heart. It is necessary to center the tube accurately (at the height of the junction of the left auricle and ventricle and 3 cm. to the left of the mid-line). On account of the distance of the tube from the plate the exaggeration of the heart silhouette by divergence of the rays is so slight as to be practically negligible (not more than 5 mm. in any direction), and the measurements of the heart shadow upon the photographic plate agree closely with the actual size of the organ.

The size of the heart silhouette increases with the age of the individual (in the absence of cardiac disease), with increasing height, and particularly with increasing weight and thoracic size. In women it is about ½ cm. smaller than in men of the same height and weight. The following table by Dietlen

outlines the normal limits above which measurements are to be regarded as indicating enlargement.

Measurements of the Orthodiagraphic Shadow in Healthy Adult Males (see Fig. 23)

Height and Weight	MR	ML	TR	TL
Height 145–154 cm (= 58–62″)..... Weight av. 47 kg. (= 103 lb.).....	3.7	8.5	12.2	13.4
Height 155–164 cm (= 62–66″)..... Weight av. 57 kg. (= 125 lb.).....	4.2	8.7	12.9	14.0
Height 165–174 cm (= 66–70″)..... Weight av. 64 kg. (= 140 lb.).....	4.3	8.8	13.1	14.2
Height 175–187 cm (= 70–75″)..... Weight av. 71 kg. (= 156 lb.).....	4.5	9.3	13.8	14.9

From the following table one may obtain the average value corresponding to the age, height, weight and circumference of the chest of any individual for comparison with the measurements in any given case. Under normal circumstances the transverse diameter of the heart should be about ½ that of the internal diameter of the thorax (more exactly 1 : 1.92).

The X-ray examination of the thorax and cardiac shadow serves to demonstrate that the position and form of the heart vary with the position of the diaphragm. If the diaphragm be very high the ovoid cardiac silhouette assumes a more horizontal position and the greatest diameter of the heart forms a larger angle with the median line. With a long thorax and low diaphragm the heart hangs almost perpendicularly, and its greatest diameter forms an acute angle with the median line. In the first case the transverse diameter of the heart (MR plus ML) is relatively large compared to the length; in the second case a small transverse diameter occurs with a greater length. The changes in form of the heart with varying positions of the diaphragm are dependent in part upon the condition of the heart muscle; such changes are more striking in the presence of myocardial damage. The heart assumes a vertical position ("dropped heart") in the asthenic type and in

Dimensions of Cardiac Shadow

	MR	ML	TR
According to height:			
154–160 cm (62–64 in.)	4.3 cm	8.5 cm	12.8 cm
160–170 " (64–68 in.)	4.8 "	8.7 "	13.5 "
170–180 " (68–72 in.)	4.8 "	8.7 "	13.5 "
180–184 " (72–74 in.)	4.4 "	9.6 "	14.0 "
According to weight:			
50–60 kg. (110–132 lb.)	4.3 "	8.3 "	12.6 "
60–70 kg. (132–154 lb.)	4.6 "	8.5 "	13.1 "
70–80 kg. (154–176 lb.)	5.2 "	8.9 "	14.1 "
According to age:			
20–30 yrs.	4.7 "	8.7 "	13.4 "
30–40 yrs.	4.9 "	8.8 "	13.7 "
40–50 yrs.	5.7 "	9.6 "	15.3 "
According to length of chest:			
80– 85 cm (32–34 in.)	4.5 "	8.3 "	12.9 "
85– 90 " (34–36 in.)	4.6 "	8.6 "	13.1 "
90– 95 " (36–38 in.)	4 9 "	9.0 "	13.9 "
95–100 " (38–40 in.)	5.0 "	9.0 "	14.0 "

many patients with pulmonary tuberculosis. In women the diaphragm tends to be somewhat higher than in men and this elevation is accentuated by abdominal distension, obesity, and pregnancy. In all such cases the heart tends to occupy a horizontal position.

Pathological changes in the heart do not always bring about alterations in the size but are particularly prone to produce variations in the form of cardiac silhouette. With enlargement of the left ventricle the cardiac shadow is enlarged particularly to the left (boot-shaped); with enlargement of the right ventricle it is more distinctly rounded or ovoid and there appears a prominence in the area of the conus arteriosus (mitral heart). Dilatation of the left auricle accentuates the third curve on the left, whereas dilatation of the right auricle brings about an accentuation of the second curve on the right and an increase in the MR diameter. Dilatation of the aorta produces a bulging in the first right curve and a conspicuous enlargement of the first left curve in the region of the great vessels.

The relative cardiac dulness as outlined by percussion should, under normal circumstances, agree closely with the cardiac silhouette obtained by orthodiagraphy. However, if the heart be enlarged to the left so that it approaches the lateral thoracic wall, or if the thorax be narrow, no such agreement is to be expected. Under the orthodiagraph the cardiac shadow is projected upon a vertical plane tangential to the anterior chest wall whereas the relative cardiac dulness is obtained by percussion upon the rounded surface of the chest

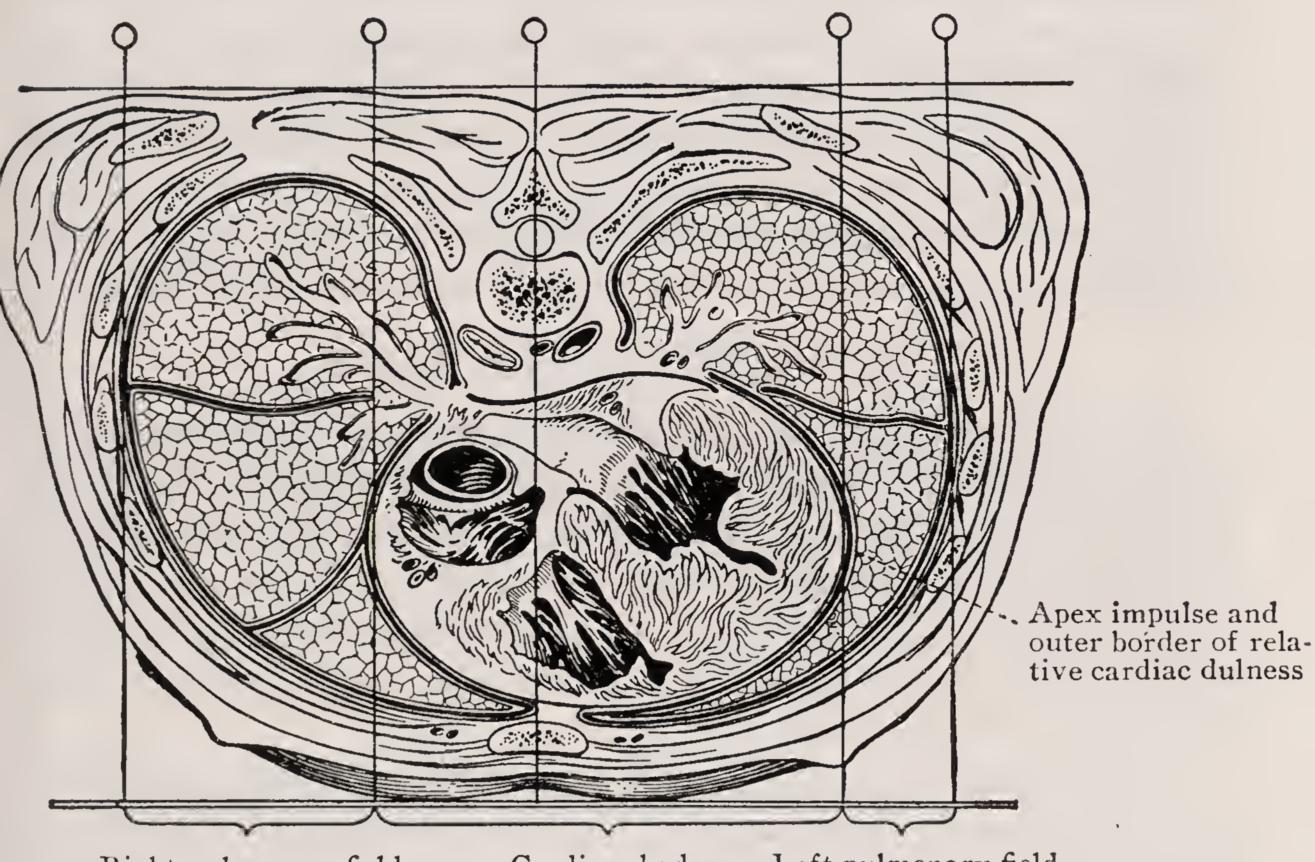


Fig. 29.—Orthodiagram projected upon a horizontal section through the thorax (after Moritz). The figure is drawn from a case of pathological enlargement of the left ventricle to illustrate that, in such a case, the apex impulse and the left border of cardiac dulness may be located on the lateral chest wall to the left of the outer border of the orthodiagraphic shadow. The small circles behind the thorax indicate the various positions of the Roentgen tube. The shadow thrown by the parallel rays is projected upon a fluorescent screen laid against the anterior chest wall.

and tends to have a distinctly greater transverse diameter. In certain cases the apex impulse may lie farther to the left than the outer margin of the orthodiagraphic shadow (see Fig. 29).

Lateral or oblique observation of the heart with X-ray may sometimes be practised to advantage, particularly in the so-called first oblique diameter with the tube placed behind the left posterior axillary line and the screen or plate against the right anterior axillary line. In the second oblique diameter the path of the rays is from the right back to the left front. In

this position the course of the aortic arch may be followed from its origin slightly to the right of, and just posterior to, the right lower border of the manubrium to its junction with the ascending aorta on the left of the vertebral column at a slightly lower level. In front of the shadow of the great vessels there may be seen a clear triangle, the anterior superior mediastinum, which is filled by the free borders of both lungs lying in front of the great vessels (vena cava, aorta, and pulmonary artery) and of the upper portion of the heart. The posterior mediastinum, lying between the spinal column and the heart just above the diaphragm, may be brought into view by oblique or transverse illumination. It is bounded in front by the auricles and through it passes the œsophagus. In addition to furnishing information concerning the size and course of the aorta and œsophagus, oblique illumination may also make possible a more accurate localization of mediastinal tumors.

AUSCULTATION OF THE HEART

Sounds arising at the mitral valve are best heard over the apex of the heart, those from the tricuspid valve at the right sternal border over the sixth costal cartilage, from the aortic orifice in the second right intercostal space or, better, over the sternum at the same level, and those produced at the pulmonic orifice in the second left intercostal space immediately adjacent to the sternum.

In the region of the heart two sounds are audible. Over the ventricles the first sound is louder and lower in pitch than the second, (its vibration frequency is 50–70 per second), over the aortic and pulmonic areas the second sound is higher and louder than the first (showing, on the average, 90 vibrations per second). The second aortic sound, as heard in the normal in the second right intercostal space, is equal in intensity to the second pulmonic sound. The first sound is produced in part by the contraction of the heart muscle and in part by the closure of the mitral and tricuspid valves. The second sounds (aortic and pulmonic) are caused by the closure of these valves. The second sound, heard over the mitral and tricuspid areas, is transmitted from the aortic and pulmonic valves. The first sound is synchronous with the apex impulse and corresponds to the beginning of ventricular systole; the

second marks the end of systole and therewith the beginning of diastole of the ventricle (see Fig. 24).

Accentuation and elevation in pitch of the first sound at the apex takes place with forceful action of the heart, e.g. after exercise and in fever. With mitral stenosis and with the so-called "irritable heart" the first sound at the apex becomes louder and higher in pitch. A decrease in intensity of the first sound is occasionally observed with aortic stenosis and mitral insufficiency. The heart sounds are strikingly diminished in intensity with exhaustion, with cardiac dilatation, with pericardial effusion and emphysema.

The second aortic sound is accentuated and of higher pitch with increased systemic blood pressure (hypertension associated with nephritis or, in some cases, with arteriosclerosis); **accentuation of the second pulmonic sound** takes place with congestion in the lesser circulation (mitral insufficiency and stenosis) and in pulmonary emphysema (interference with the pulmonary circulation). With disease of the mitral valve the second pulmonic sound may not be abnormally loud if there be a coincident tricuspid insufficiency. A condition in which the heart sounds follow each other with a regular tic-tac rhythm is spoken of as **embryocardia.** This phenomenon is sometimes observed with myocardial failure. Here the pauses between the individual tones are equal in length.

Splitting of the heart sounds often occurs in healthy individuals in certain phases of respiration; it is, therefore, not always a sign of disease. In certain cases of mitral stenosis the second sound may appear to be doubled. The occurrence of a dull tone, either in the first portion of diastole or shortly before the first sound, is characteristic of a **gallop rhythm.** This occurs in some cases of hypertrophy or dilatation of the left ventricle and is most common with the hypertension associated with contracted kidneys; under these circumstances it is to be regarded as an ominous sign. With heart failure in the course of typhoid fever or hyperthyroidism gallop rhythm may sometimes appear. In a graphic record of the apex beat it may be demonstrated that, corresponding to the third sound, there is a definite wave in diastole, or the auricular

wave immediately preceding ventricular systole may be abnormally high.

Cardiac Murmurs

These are to be differentiated from the heart sounds by the fact that, whereas the latter are short in duration and rapidly subside, being produced by the vibrations of valves and heart walls, murmurs are composed of repeated and protracted vibrations. The heart sounds are to be compared to the tone

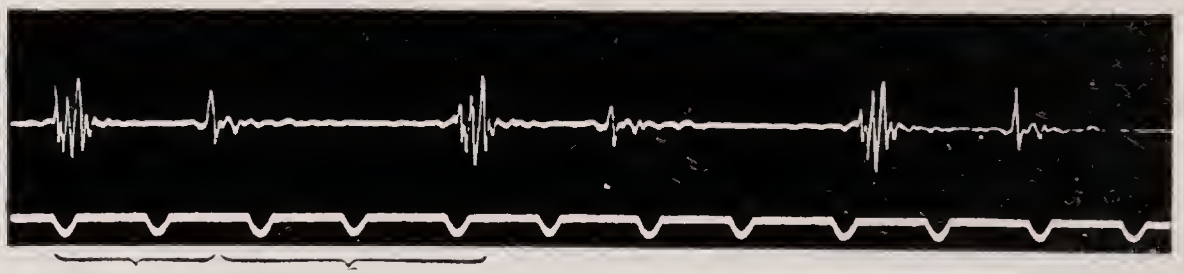


FIG. 30.—Normal heart sounds. Time below in 1/5 sec.

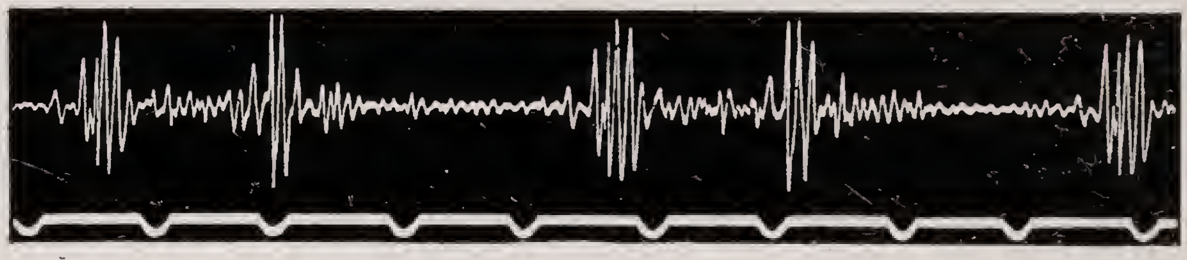


FIG. 31.—Systolic and soft diastolic murmur with mitral insufficiency and stenosis.

produced by **plucking** a violin string and the murmurs to that elicited by **bowing** the string.

The shorter duration of the heart sounds and the longer duration of the murmurs, which may completely fill the pause normally present between the sounds, may be visualized by the method of Einthoven. In this method the sounds are transmitted to a microphone, and the vibrations in the microphone recorded electrically by means of a string galvanometer. The movements of the galvanometer string may be photographed upon a plate or film.

A murmur is designated as **systolic** when it occurs between the beginning of the first sound and the beginning of the second, and as **diastolic** if it occupies any portion of the pause

between the second sound and the succeeding first sound. A murmur occurring late in diastole and continuing up to the next first sound is sometimes designated as **presystolic.** In the presence of murmurs the heart sounds may be clear, or more or less obscured. A murmur may be whistling, blowing, or rumbling, but its quality is far less important than the timing of the murmur relative to the heart sounds, i.e. its position in systole or diastole, and the portion of the præcordium over which it is of greatest intensity. Murmurs show a vibration frequency varying, of course, with their pitch but lying usually between 60 and 130 per second.

The **intensity of a murmur** is proportional to the velocity of the blood stream and the diameter of the orifice at which it is produced, and is also dependent upon the smoothness or roughness and capability of vibration of the portions of the heart or great vessels in the neighborhood. **Murmurs are best transmitted in the direction of the blood stream by which they are produced.** The systolic murmur of aortic stenosis is for this reason transmitted into the carotid artery whereas the diastolic murmur of aortic insufficiency, on the other hand, is transmitted, not into the carotid, but downward along the left sternal border toward the apex of the heart.

A **systolic** murmur at the mitral or tricuspid areas occurs with insufficiency of the valve; systolic murmur at the aortic or pulmonic areas with stenosis of the orifice.

Diastolic murmurs at the mitral area indicate stenosis, at the aortic and pulmonic areas insufficiency. In general, diastolic murmurs are of greater significance than systolic in the diagnosis of valvular disease.

Murmurs are classified as organic and functional; the latter are nearly always systolic and are no indication of anatomical lesions. It is not uncommon to meet with a functional murmur over the pulmonic area under conditions of rapid and forceful cardiac action, particularly if associated with dilatation of the ventricle, as with high fever, hyperthyroidism, anæmia, leukæmia, and irritable heart. Occasionally in pernicious anæmia a functional diastolic murmur may be observed which may disappear with improvement in the blood picture. Functional murmurs may be distinguished from organic murmurs by the absence of the other evidences of valvular disease

and by the fact that they disappear upon the improvement of the anæmia, fever, hyperthyroidism, etc. It is sometimes extremely difficult, however, to determine whether a systolic murmur over the mitral area be functional or organic.

Pericardial friction sound is caused by a roughening of the serous membrane by fibrin deposit, usually as a result of pericarditis, and more rarely by tubercle or metastatic tumor nodules upon the pericardium. Characteristically a pericardial friction sound occurs only in certain phases of the cardiac cycle (usually at the end of systole and the beginning of diastole), is sharply localized, rough and superficial (sounding often as though directly below the stethoscope bell). It is sometimes divided into phases corresponding to a gallop rhythm. Such friction murmurs are altered in intensity by change in position of the patient, and sometimes by deep inspiration. Endocardial murmurs may be present at the same time, often more or less obscured by the pericardial sounds.

Extrapericardial (pleuropericardial) friction sound is produced by friction between the outer layer of the pericardium and the visceral pleura. This is synchronous with the heart beat but undergoes a rhythmic accentuation with respiration which may be eliminated by directing the patient to hold his breath. The extrapericardial friction is in reality a sign of pleurisy rather than of pericarditis. With mediastinal emphysema crackling râles are heard over the præcordium synchronous with the heart beat.

Particularly in children and young adults murmurs may occasionally be audible with the patient lying on his back but inaudible in other positions. These so-called **"accidental murmurs"** are most frequently heard in the pulmonic area, are systolic in time, and are of little diagnostic significance.

Auscultation of the Blood Vessels

Over the carotid and subclavian arteries two tones are heard with each heart beat; the first corresponds to the systole of the heart and therefore to the distension of the arteries, and the second to the diastole of the heart (closure of the aortic valve) and collapse of the artery. The first tone is caused principally by the distension and stretching of the

arterial wall, the second is simply the transmitted second aortic sound. This second sound is sometimes absent from the carotid or subclavian in cases of aortic insufficiency. With aortic stenosis, with dilatation or aneurysm at the base of the aorta and sometimes with fever there is an audible **systolic murmur** over the carotid artery.

Over the **peripheral arteries** (femoral, brachial, radial) no tone is audible in the normal individual. Upon pressing the artery with a stethoscope there may be elicited a murmur synchronous with the pulse wave or upon further pressure a dull sound. Such a dull sound may be audible without pressure over the peripheral arteries in cases of aortic insufficiency, hypertension or irritable heart. Upon light pressure with a stethoscope in such cases there may be elicited a double murmur, the so-called Duroziez's sign. With hyperthyroidism a systolic murmur is sometimes audible over the thyroid gland and particularly over the superior and inferior poles at which its arteries enter. Auscultation of the **carotid** is carried out just above the clavicle and lateral to the lower end of the M. sternocleidomastoid or at the inner border of this muscle at the level of the thyroid cartilage. The **subclavian** may be ausculted in the infraclavicular fossa at the mid-clavicular line or in the outer portion of the supraclavicular fossa.

With insufficient filling of the jugular vein there may be audible over the lateral border of the sternocleidomastoid muscle a continuous sighing murmur (Bruit de diable), which becomes louder with inspiration and upon drawing the head to the other side. A similar murmur may be audible over the femoral vein in cases of severe anæmia.

ESTIMATION OF THE BLOOD PRESSURE (SPHYGMOMANOMETRY)

The arterial blood pressure may be measured by means of the sphygmomanometer of Riva-Rocci which consists of an inflatable, broad rubber cuff which encircles the upper arm of the patient and may be made to compress the brachial artery. The cuff of Recklinghausen, which is 12 cm. in width, is connected with a mercury monometer or with an anæroid device by means of rubber tubing. Through a second rubber

tube air is pumped into the cuff until the radial pulse is no longer felt. The air is then gradually released and the systolic pressure roughly estimated as the pressure at which the radial pulse again becomes palpable.

The systolic pressure and the diastolic as well may be more accurately determined by means of auscultation over the cubital artery peripheral to the compressing cuff (Korotkoff and Fellner). As long as the pressure in the cuff is so great as to collapse the artery completely no sound is heard

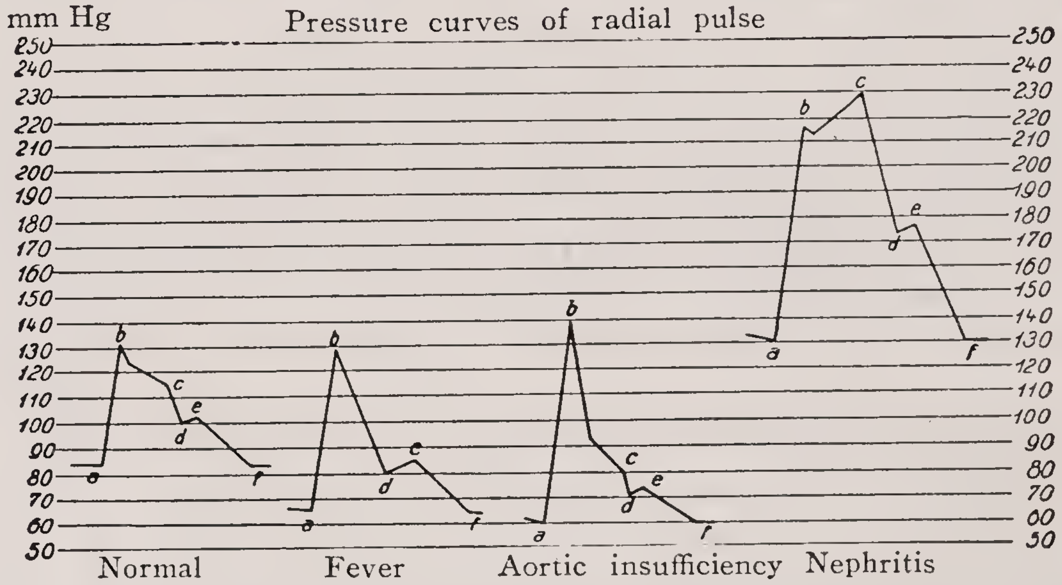


FIG. 32.—Pressure curves from the radial artery. a-b ascending limb, b peak of first systolic wave, c second systolic or predicrotic wave, c-d postsystolic fall in pressure, d beginning of dicrotic wave, e peak of dicrotic wave, f diastolic pressure level, d-f diastolic portion of pulse curve.—In the last curve (Hypertension) the c wave is on the ascending limb and represents a pressure considerably higher than that in the preceding curves. This anacrotic type of pressure curve is found with increased peripheral resistance. It is to be noted that with any given ventricular output the pressure in the artery rises higher if it still be filled or distended at end of the previous diastole or when the optimum arterial distension is exceeded. Thus with a high diastolic pressure, e.g. in hypertension the same ventricular output will bring about a greater rise in pressure than with a low diastolic pressure, e. g. in fever.

over the cubital vessel; as soon, however, as the pressure in the cuff falls to a point at which the pulse wave comes through beneath it a sound becomes audible over the cubital artery; this point represents the systolic pressure. As the pressure continues to fall the arterial sound gradually becomes louder and then suddenly decreases in intensity. The pressure level corresponding to this sudden change in intensity represents the diastolic or minimal pressure.

In the normal individual the systolic pressure as measured in the brachial artery by this method lies between 100 and 140 mm. of mercury, (1.36–1.9 meters of water), the diastolic pressure 60–80 mm. of mercury, (0.8–1.0 meters of water).

The difference between the systolic and diastolic pressures is designated as the **pulse pressure**; it corresponds to the amplitude of the pulse and amounts, in the normal, to from 50–60 mm. of mercury (68–95 cm. of water).

The venous pressure in the arm, measured at the level of the heart, amounts in the normal (Moritz and Tabora) to 3–6 mm. of mercury, (4–6 cm. water). With congestive heart failure the venous pressure may rise to 15–23 mm. of mercury. The pressure in the capillaries is variable but amounts, on the average, to about 30 mm. of mercury. By many authors the venous and capillary pressures are expressed in terms of water rather than mercury. Translation of these values may be accomplished by the following formulæ:

1 mm. Hg. = 13.6 mm. H_2O, 10 mm. H_2O = 0.73 mm. mercury.

Pathological elevation of the blood pressure to 200, 250 or even 350 mm. Hg (hypertension) occurs with any increased resistance in the arterioles and capillaries to the outflow from the arteries (provided the functional capacity of the left ventricle be unimpaired). If, on the other hand, the myocardium be incapable of maintaining such a pressure (e.g. with myocardial degeneration) the entire circulation is slowed and stasis occurs in the lungs and veins. On the contrary, provided the smaller arteries and capillaries are of normal calibre, an increase in the circulatory rate with an acceleration of the pulse, (e.g. in violent exercise) may take place without notable change in the blood pressure. Narrowing of the peripheral arteries and particularly of the arterioles may occur either as a result of concentric thickening of the vessel wall, which may advance to complete obliteration of the lumen (endarteritis, arteriolosclerosis), or, not infrequently, by contraction of the musculature in the vessel wall through the action of the vasomotor nerves. Transient and widespread contraction of the arterioles causing a conspicuous increase in blood pressure, particularly in diastolic pressure, occurs in lead poisoning, during rigor, in certain forms of acute nephritis and following the administration of adrenalin. A persistent elevation of blood pressure occurs in many forms of chronic nephritis, particularly with contracted kidney, and also sometimes at the menopause, with myomata uteri and in

certain types of heart disease during the stage of decompensation. With long-standing hypertension the ventricle becomes hypertrophied; its load is increased by the increase in intra-aortic pressure against which the ventricular contents must be discharged. With valvular disease the blood pressure is not conspicuously altered in the absence of circulatory insufficiency. In fever the diastolic pressure is usually abnormally low since, as a result of diminished vascular tone, the outflow through the arterioles and capillaries is facilitated; here, in the absence of circulatory insufficiency, as long as the systolic pressure remains high the pulse pressure is increased (see Fig. 32); if, however, dilatation of the heart supervene the systolic pressure falls and the pulse becomes small and soft. The blood pressure may be very low (100 or 90) in nervous or exhausted individuals and tends to be extremely low in collapse and in Addison's disease.

THE ELECTROCARDIOGRAM

With each excitation of an excitable tissue there is produced an electrical current of such a nature that the excited point is apparently electro-negative to the remaining unexcited portions of the tissue. This, the so-called action current, occurs with every excitation of striated or cardiac muscle and tends to assume a definite form. The action current of the heart is conducted to all portions of the body and may be lead off from the extremities to a galvanometer. Although the voltage of this current is extremely low it may be recorded with the sensitive Einthoven string galvanometer. This instrument consists of a delicate quartz or platinum filament, through which the action current is conducted, and which is suspended between the poles of a powerful electro magnet. The deflection of the string produced by the passage of the action current may be recorded by projecting its shadow, by means of an optical system, upon a rapidly moving photographic film.

It is customary in recording the action current of the heart to utilize three leads:

I Right arm and left arm,
II Right arm and left leg,
III Left arm and left leg.

Electrodes of lead or german-silver are placed about the extremity between layers of bandage moistened with salt solution, and connected to the string galvanometer. The curves obtained by the different leads from the same individual show certain characteristic differences since the potentials are very dependent upon the axis of the lead. In certain pathological abnormalities of the cardiac rhythm the electrocardiogram may show striking and characteristic departure from the normal.

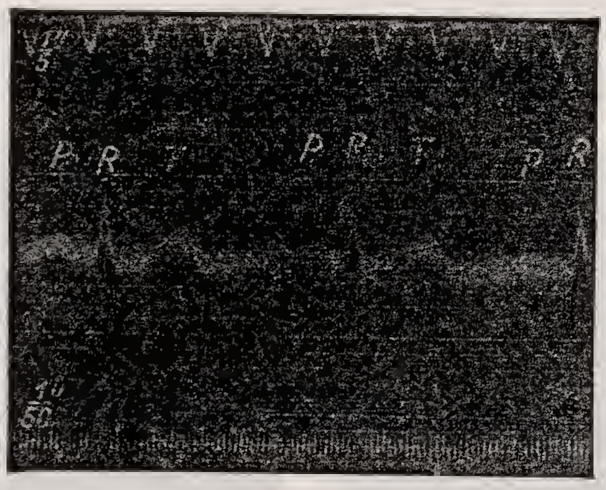


FIG. 33.—Normal electrocardiogram.

In the normal electrocardiogram several waves are distinguished (Fig. 33):

P wave—a small upright deflection associated with auricular excitation.

Q, R and S waves—corresponding to the excitation of the ventricle, Q and S being downward and R upright.

T wave—occurring after an interval following the Q R S complex, a long, flat wave the end of which marks the end of ventricular systole.

It must be pointed out that the P and R waves indicate the **excitation** of auricle and ventricle respectively and are not absolutely synchronous with the **contractions** of these chambers.

Under normal circumstances the several waves of the electrocardiogram are separated by definite intervals of time. The normal values for adults are as follows:

P–R interval	.10–.16 sec.
Q R S interval	.06–0.1 sec.

Lengthening of the P–R interval indicates a delay of the conduction of the excitatory process from auricles to ventricles. Increase in the Q R S interval above the normal is a sign of impaired intra-ventricular conduction. It is frequently associated with disease of the heart muscle, and occurs also with advanced coronary disease. Certain deviations from the normal configuration of the electrocardiogram, even though the rhythm remain unaltered, are occasionally associated with organic cardiac disease, and may be of diagnostic significance. Thus the P-wave is sometimes abnormally high in cases of long standing mitral stenosis associated with distension or hypertrophy of the auricles.

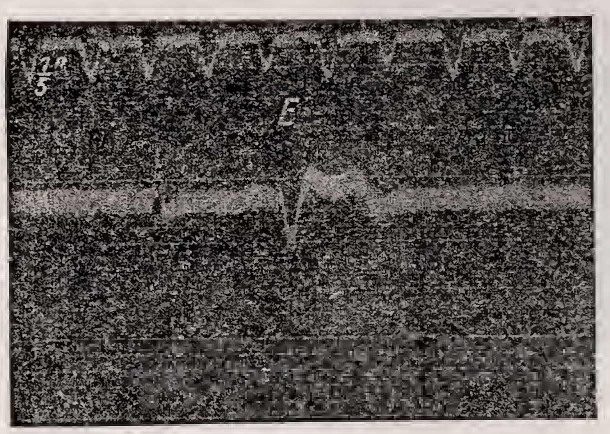


FIG. 34a.—Electrocardiogram showing left ventricular extrasystole.

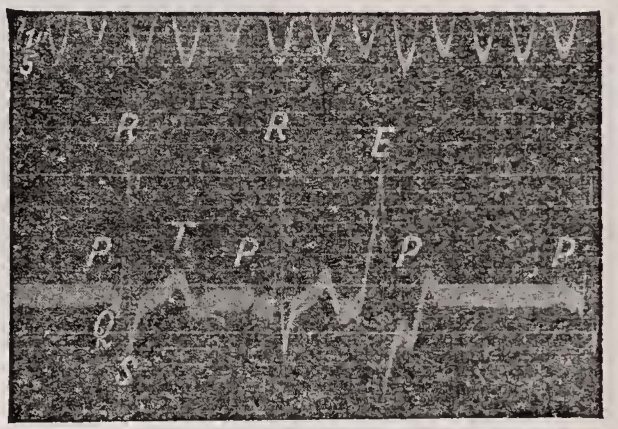


FIG. 34b.—Electrocardiogram showing right ventricular extrasystole.

The R-waves under normal circumstances vary in height depending upon the lead. According to Einthoven's law the sum of the heights of the R-waves in leads I and III should equal the height of that in lead II ($R_1 + R_3 = R_2$). Under pathological conditions, and particularly if one side of the heart or the other be conspicuously hypertrophied, this relation of the R-waves may be altered. Thus preponderance of the left ventricle, as in the case of aortic insufficiency or hypertension, is commonly associated with a high R-wave in the first lead and a low S-wave in the third. Conversely, with outspoken hypertrophy of the right ventricle, S_1 is unusually deep and R_3 abnormally high, e.g., in some cases of mitral stenosis, congenital pulmonary stenosis. In infants, for a short time after birth, the electrocardiogram is of the type associated with right ventricular preponderance.

Under pathological conditions the P wave may be absent

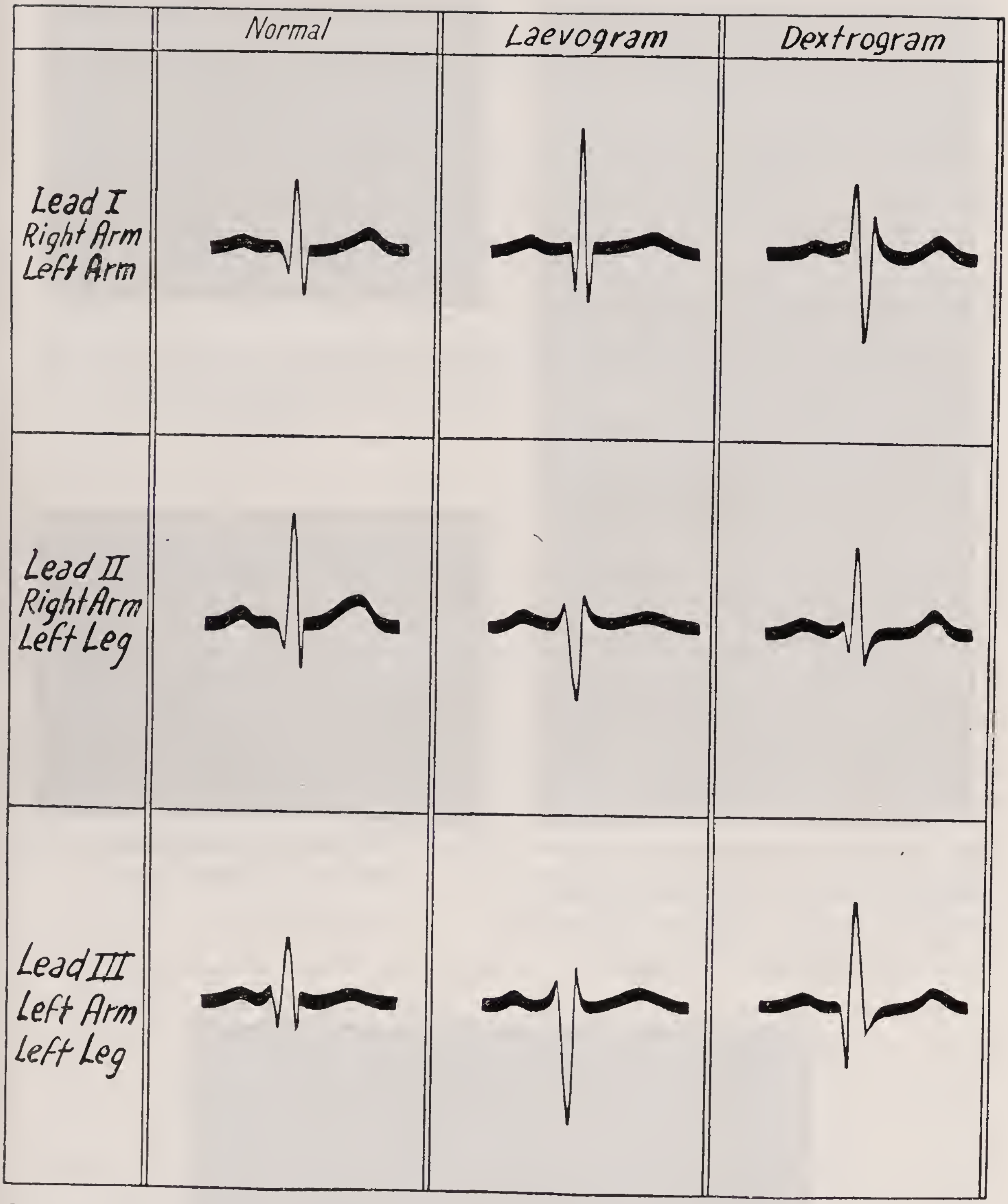


FIG. 35.—Electrocardiogram. In the normal electrocardiogram $R_1+R_3=R_2$ (Einthoven's Law). The laevogram is characterized by high R in Lead I and low S in Lead III. It is frequently associated with hypertrophy of the left ventricle (hypertension and aortic insufficiency). The dextrogram is distinguished by low S in Lead I and high R in Lead III. It is normally encountered in records taken from infants (up to 4 months of age) and occurs also in association with certain congenital cardiac abnormalities.

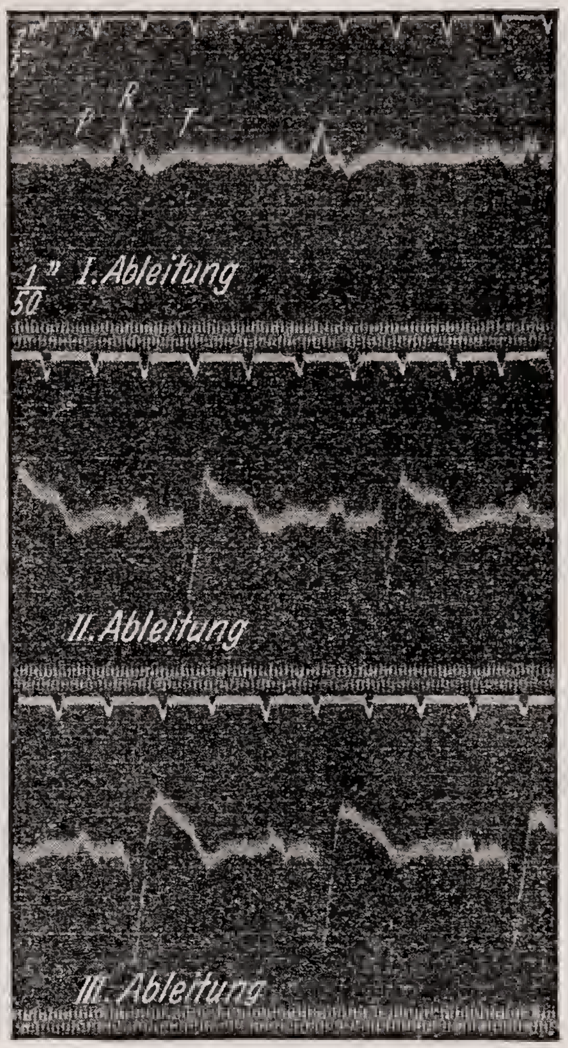


Fig. 36.—Electrocardiogram in case of extensive myocardial degeneration (bundle-branch block). Prolonged P–R interval, QRS complex widened. Splintering of QRS complex in Lead I. QRST inverted in Leads II and III.

Fig. 37a.—Auricular flutter with irregular ventricular response. Between the R waves are visible the rapid and regular P waves.

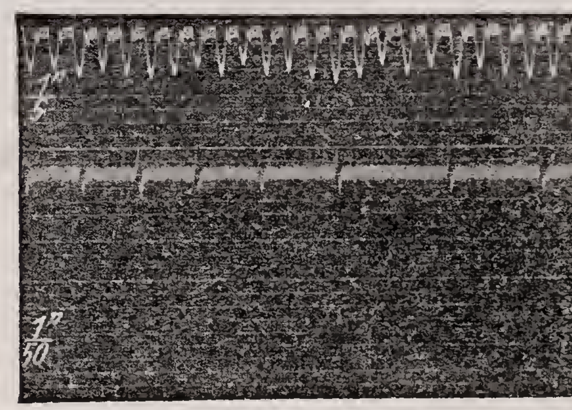


Fig. 37b.—Auricular fibrillation. Total absence of visible P waves.

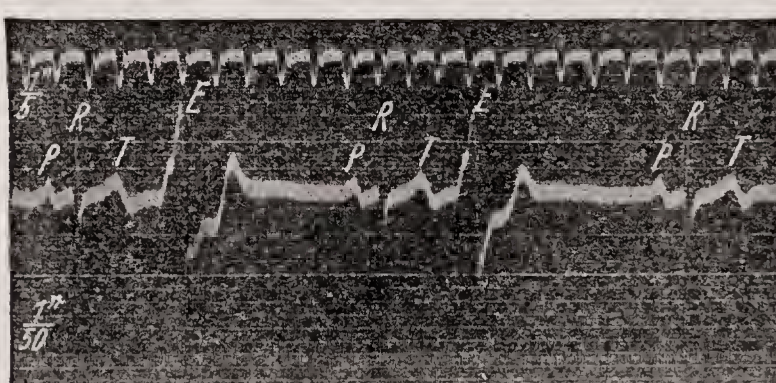


Fig. 38.—Ventricular extrasystoles in bigeminal sequence.

when auricular excitation either fails to take place or occurs so rapidly and irregularly that it cannot be recorded (auricular fibrillation). **Auricular flutter** is characterized by very rapid auricular excitations (200–400 per minute), which produce regularly-spaced, small waves in the electrocardiogram. With auricular fibrillation ventricular excitation takes place irregularly and the R waves occur at the extremely irregular intervals characteristic of arrhythmia perpetua. In the case of hypertrophy of the **left** ventricle (with aortic insufficiency) the R wave is abnormally high in lead I and the S deep in lead III; with **right** ventricular hypertrophy, on the other hand, SI is deep and RIII high. The P wave may be unusually prominent in cases of mitral disease. In certain cases of severe myocardial damage the smooth rapid rise and fall of the Q R S complex may be notched or prolonged, or the final deflection, T, may be inverted or altered in form. **Extrasystoles** arising in various portions of the heart produce characteristic changes in the electrocardiogram. When such arise in the ventricle the record assumes the form illustrated in figure 34 in which type A represents the record of a right ventricular extrasystole arising near the base of the heart and type B a left ventricular extrasystole arising near the apex (leads I and II). In the case of an extrasystole arising in the A–V bundle or in the upper portion of the His bundle the electrocardiogram of the ventricle shows a normal Q R S complex and T wave and is to be recognized only by its prematurity and by the absence of an auricular complex preceding it. Auricular extrasystoles are characterized by atypical and premature P waves but produce otherwise no abnormalities in the electrocardiogram. Extrasystoles arising in the lower portion of the auricles, i.e., near to the A–V node, are sometimes associated with negative P-waves and an unusually short P–R interval.

THE PULSE

The pulse is described according to the following qualities: Rate (P. frequens or rarus); Size (P. magnus or parvus); Tension (P. durus or mollis); Type of wave (P. celer or tardus); Rhythm (P. regularis or irregularis).

The **rate** in the healthy adult at rest is 60–80 per minute, in children 90–140 and in the aged from 70–90.

Slowing of the pulse—bradycardia, pulsus rarus, occurs during convalescence from certain infectious diseases, e.g. influenza, with disturbances of digestion, particularly with those associated with vomiting, with icterus (due to the action of the bile acids upon the heart), with **vagal stimulation,** with increased intracranial pressure (e.g. in the first stage of a basilar meningitis) and, among the valvular defects, almost exclusively with aortic stenosis.

Acceleration of the pulse—tachycardia, pulsus frequens, occurs normally during and after exercise, after taking food, and usually during convalescence. Under pathological conditions in fever (the pulse increases in rate approximately 8 beats per degree C. elevation of temperature), with **vagus**

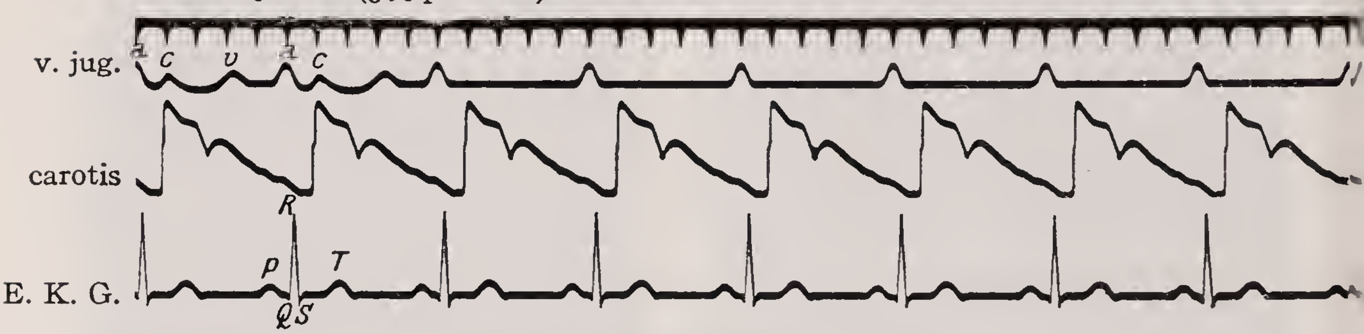


FIG. 39.—Normal cardiac rhythm.

paralysis and with excessively increased intracranial pressure (e.g. in the later stages of basilar menigitis). Rapid pulse may be temporarily present with irritable heart and persistently so with hyperthyroidism. It is an important sign of cardiac failure and is characteristically present in collapse.

Paroxysmal tachycardia is characterized by a rapid, regular rhythm (up to 250), which begins suddenly, ends abruptly, and is characteristically uninfluenced by change in position or by pressure upon the vagus in the neck.

The **size** of the pulse (pulsus magnus or parvus), as palpated by the finger or recorded by the sphygmograph is less dependent upon the dilatation of the artery itself than upon the increase in pressure during filling and the decrease during collapse of the artery, the so-called pulse pressure. The arterial pulse is to be regarded as a **wave of pressure** rather than of volume. The pulse wave is, therefore, larger the

greater the volume of blood thrown out from the left ventricle (volume output) and the more rapidly the blood flows out of the arteries. A pulse of large volume occurs with aortic insufficiency, nephritis and often in fever provided the left ventricle is competent. (It is also observed in certain cases of hyperthyroidism. Ed.)

A small pulse is observed with myocardial insufficiency, collapse, with stenosis of any cardiac orifice and during a chill. The size of the pulse may be judged more or less accurately by determination of the systolic and diastolic pressure.

Tension (P. durus or mollis), i.e. the distension of the artery as distinguished by the resistance offered to the palpating finger; a pulse of high tension may be obliterated only with difficulty. The pulse tension corresponds to the blood pressure. Under normal conditions the radial pulse is palpable only during systole, i.e. when the intra-arterial pressure is between 100 and 120 mm. of mercury, and not during diastole when the pressure falls to 60–70 mm. of mercury. If the diastolic pressure be above 100 the artery may be felt as a distended tube throughout the pulse cycle. It is possible to estimate the pulse tension approximately by the application of gradually increasing pressure with the finger over the radial artery, at the same time palpating the artery at a point distal to that at which pressure is applied. A far more accurate method of measuring is that by means of the sphygmomanometer. If the systolic and diastolic blood pressures are both elevated the artery feels hard, like a lead wire. A pulse of high tension is present in all cases of hypertension, e.g. with some forms of nephritis, particularly with contracted kidney, with lead poisoning and arteriolarsclerosis. A soft pulse is observed with infectious diseases, tuberculosis, cardiac failure and anæmia.

The tension of the pulse is not to be confused with thickening of the arterial wall. In arteriosclerosis the intima may be irregularly thickened and sometimes contains deposits of calcium salts. Under these conditions the arterial wall may feel, to the examining finger, as though beset with irregular thickenings ("goose-neck" artery). Thickening may sometimes occur in the medial coat and such thickening is most easily detectable if the blood be forced out of a segment of the

artery and the empty vessel be palpated. With any considerable thickening of the arterial wall estimation of the compressibility of the pulse by palpation is very difficult.

The **form** of a pulse wave (P. celer or tardus), i.e. the rapidity with which the pulse pressure increases and decreases. The sphygmographic record of pulsus celer shows a steep, pointed wave while that of pulsus tardus (aortic stenosis) is low and flat (Figs. 41–45). With pulsus celer, as for example with aortic insufficiency, the difference between the systolic and diastolic pressures is unusually large (80-100 mm. Hg. as contrasted with 50–60 mm. in the normal).

The **rhythm** (P. regularis or irregularis). Under normal conditions the heart beats regularly and this regularity is maintained in many pathological conditions. Irregularities of the rhythm may occur with various types of cardiac disease but are not in themselves signs of myocardial insufficiency, although certain types of irregularity may seriously interfere with the efficiency of the cardiac function, e.g. auricular fibrillation. At one time it was incorrectly assumed that irregularity of the heart beat and therefore of the pulse was pathognomonic of disease of the heart muscle (myocardial degeneration or myocarditis). As a matter of fact the cardiac rhythm may be absolutely regular in the presence of severe myocardial disease.

The following types of **cardiac irregularities** are to be distinguished:

Sinus arrhythmia in which the rhythm changes more or less abruptly from a slow to a fast rate and vice versa; the most familiar example of this type is the so-called respiratory arrhythmia: In the healthy individual the cardiac rate may quicken during a deep inspiration and become considerably slower during expiration. This type of arrhythmia is particularly common in infants. It is due, apparently, to increased tone on the part of the vagus. In individuals with particularly sensitive nervous control of the heart such an arrhythmia may develop with change in position (lying to standing) with emotional disturbance or even with exercise.

The **extrasystolic irregularities.** An **extrasystole** is a premature beat occurring independently of normal rhythm and arising in some other portion of the heart than the sinus node

(e.g. auricle, A.–V bundle or from some point in the ventricular musculature). Extrasystoles may be due to an increased irritability on the part of localized portions of the heart. With those arising in the ventricle, the normal ventricular systole immediately following is usually lacking, since the auricles continue to beat in a normal rhythm and the succeeding impulse conducted from the auricle finds the ventricle unexcitable (refractory period). For this reason a ventricular extrasystole is followed by an abnormally long **compensatory pause** after which the normal sequence is resumed. In the case of auricular extrasystoles the compensatory pause is usually shorter or may be lacking entirely. With nodal extrasystoles the auricular and ventricular systoles may occur simultaneously resulting in characteristically large and sharp jugular pulse waves. Extrasystoles are sometimes associated with an abnormally forceful cardiac impulse so that the patient may complain of a sensation of pounding, or sometimes that the heart for a period ceases to beat. If the extrasystoles occur regularly following each normal systole there results the so-called **pulsus bigeminus** in which, after every normal pulse, following a short pause there is a smaller pulse wave. With heaping of extrasystoles the pulse may be extremely irregular. Extrasystolic irregularities are not an absolute sign of severe cardiac disease but may occur after certain intoxications, e.g. with excessive use of tobacco, or after infectious diseases, or with certain nervous or vasomotor disturbances. They may sometimes be associated with myocardial disease. Extrasystolic irregularities account for the larger proportion of cardiac arrhythmias. An accurate conclusion as to the particular type of extrasystole and indeed of cardiac arrhythmia is only possible if the ventricular beat be recorded by means of an apex or carotid tracing and that of the auricle by means of a jugular tracing. Most accurate in the description and analysis of cardiac arrhythmias is the electrocardiogram.

Pulsus irregularis perpetuus (auricular fibrillation) is characterized by complete irregularity of the pulse associated with absence of the normal auricular wave in the jugular pulse and of the P wave in the electrocardiogram. With this condition there may be distension of the right auricle. This form of arrhythmia may continue for a long period of time or may

Time in 0.2 sec. (300 per min.)

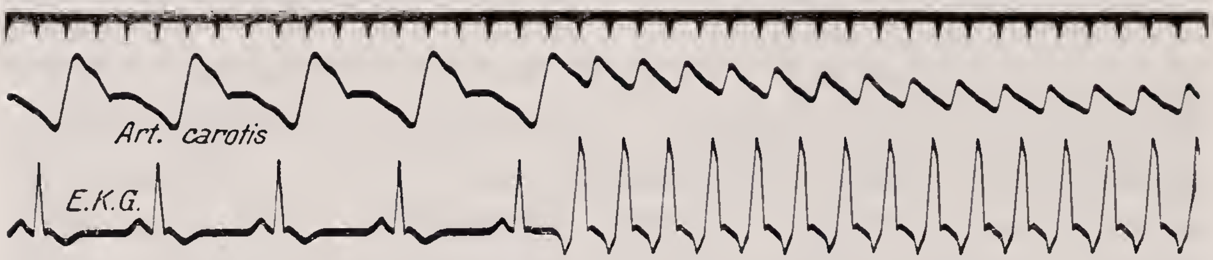


FIG. 40.—Onset of paroxysmal tachycardia.

Time in 0.2 sec. (300 per min.)

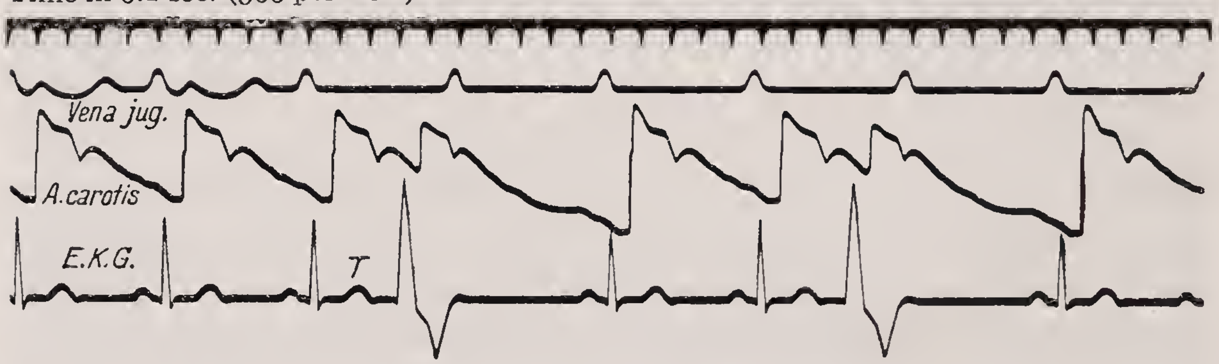


FIG. 40a.—Ventricular extrasystoles.

Time in 0.2 sec. (300 per min.)

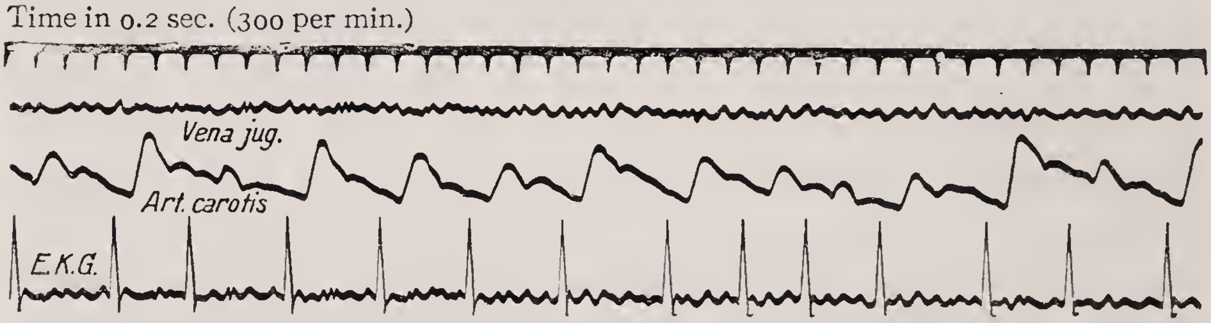


FIG. 40b.—Arrhythmia perpetua (auricular fibrillation).

Time in 0.2 sec. (300 per min.)

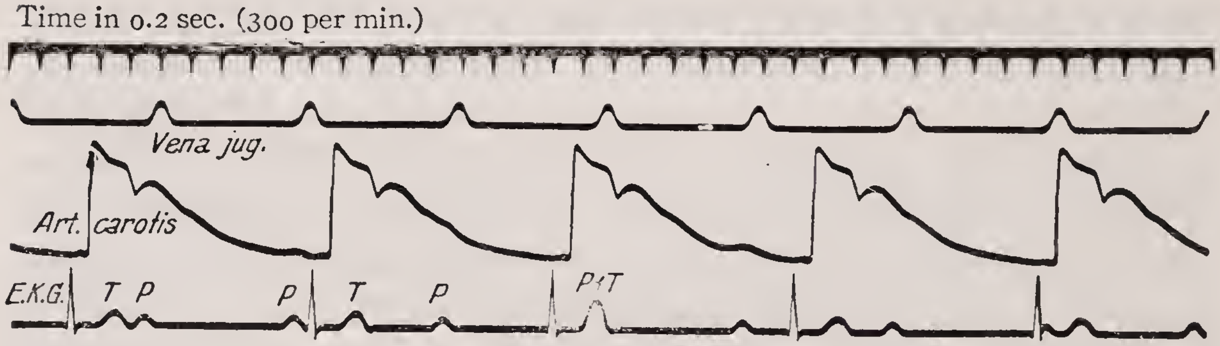


FIG. 40c.—Complete block.

Time in 0.2 sec. (300 per min.)

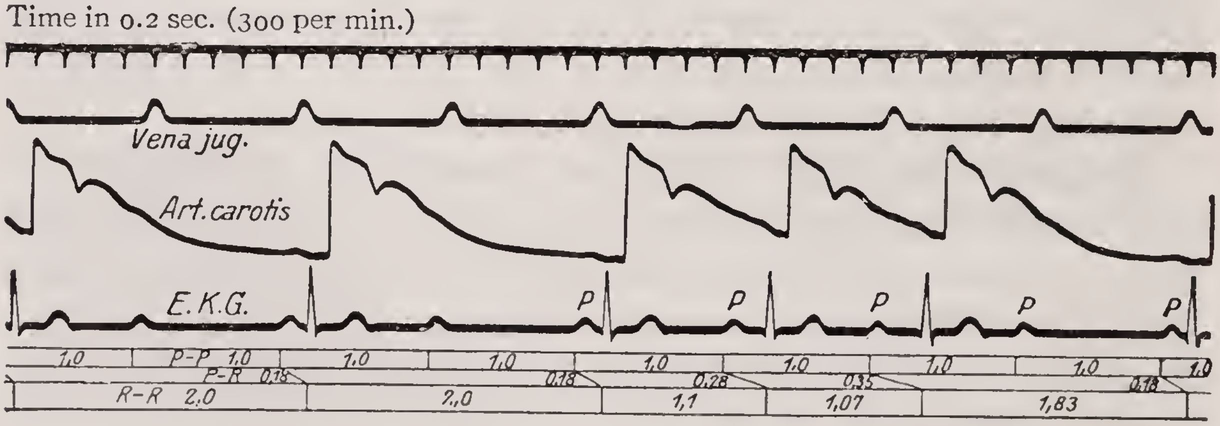


FIG. 40d.—Partial block.

occur in paroxysms of hours' or days' duration. It is sometimes possible to count the rate of auricular excitation in this condition in the electrocardiogram. In **auricular flutter** the auricular excitations are greatly accelerated (around 300) but are more regular and less rapid in rate than in auricular fibrillation. In auricular fibrillation the normal regular impulses from the auricles to the ventricles are lacking and the ventricular beat is extremely irregular. In auricular flutter the auricular excitations occur at a rate so rapid that only one in two or more finds the ventricle excitable. In pure flutter the ventricular rhythm is regular at a rate one half, one third, etc. that of the auricle.

Abnormalities of conduction in the His bundle bring about abnormally long intervals between auricular and ventricular systoles. In certain types of block this interval becomes progressively longer with each cardiac cycle until a ventricular systole drops out. During this longer pause the conductivity of the conduction system so improves that the next A–V interval is shorter; the series is then repeated. Such an irregularity may assume the form of pulsus trigeminus. With another type of disturbance of conduction ventricular contraction follows only every second or third auricular beat so that the arterial pulse is greatly slowed and occurs, in comparison to the jugular pulse, at a rhythm of 1:2 to 1:3. With complete interruption of the A–V bundle, e.g. by scar tissue or gumma, complete auriculo-ventricular dissociation (heart block) may occur. The auricles beat with their normal rhythm but the ventricles beat independently at their own slower tempo, usually about 30 per minute. In many cases of bradycardia the reduction of the pulse rate may be even greater; during a paroxysm this may fall to 12 or even 7 per minute. With these attacks of extreme slowing of the pulse transient loss of consciousness may occur (Adams–Stokes syndrome).

In **pulsus alternans** the pulse is absolutely regular in rhythm but its amplitude is alternately reduced. Genuine pulsus alternans, which may sometimes be confused with pulsus bigeminus (produced by extrasystoles), is a sign of **myocardial failure.**

If extrasystoles occur early following a ventricular contraction so that ventricular filling is incomplete the premature

contraction may not be able to open the aortic valves against the pressure in the aorta; there results no pulse wave in the artery and the second sound is absent.

(In auricular fibrillation a similar condition may arise so that a certain number of ventricular contractions fail to produce a pulse. The difference between the apical and radial rate, under these circumstances, (simultaneously counted) is known as the **pulse deficit.** Ed.)

In **pulsus paradoxus** the arterial pulse becomes smaller with inspiration and with deep inspiration may become impalpable; it is observed with extensive adhesions or tumors of the mediastinum. Inequality of the right and left radial pulses may be due to the asymmetry of origin or diameter of the subclavian arteries or, more often, to narrowing of these arteries at their origin from the innominate or aorta, e.g. with arteriosclerosis or aneurysm of the aorta.

Sphygmography

In the pulse curve recorded by the sphygmograph several waves are distinguished: A short preliminary deflection (isometric interval) an ascending limb which corresponds to the ejection of blood from the heart into the arteries. A second flat, pre-dicrotic wave follows this first but is still within the period of systole. With the end of ventricular systole and the closure of the aortic valves the arterial curve undergoes a steep fall interrupted by a notch (dicrotic notch) due to rebound coincident with closure of the aortic valves. From this point the curve falls gradually during the remainder of diastole as the artery empties through the capillaries. At the end of the diastolic portion of the curve there may occur a flat wave produced by auricular contraction.

Such a pulse curve is only to be obtained from the arteries adjacent to the heart, the aorta, carotid and subclavian (see Fig. 35). In the peripheral arteries, e.g. the radial artery, the pulse curve is somewhat deformed by peripheral influences: The first systolic wave is usually sharper and marks the highest point of the curve. The curve is sometimes more or less modified in the process of registration due to over-swing of the recording pen. The predicrotic wave is usually far less pro-

nounced in the radial tracing than in the carotid or may indeed be wanting in the former; this is not uncommonly observed with a relaxed peripheral field which makes possible a rapid outflow from the arteries, e.g. in fever. If, on the other hand, the outflow into the periphery is impeded by vascular spasm or sclerotic narrowing of the smaller arteries the predicrotic wave may appear sharply in the radial pulse; it may be more striking and even higher than the systolic wave. Such a pulse curve is spoken of as **anacrotic.**

The post-systolic fall in pressure and the succeeding dicrotic notch are more pronounced in the radial pulse than in the carotid. This fact has led to doubt as to whether the dicrotic notch in the peripheral arteries be identical with the wave in the carotid tracing which is synchronous with closure

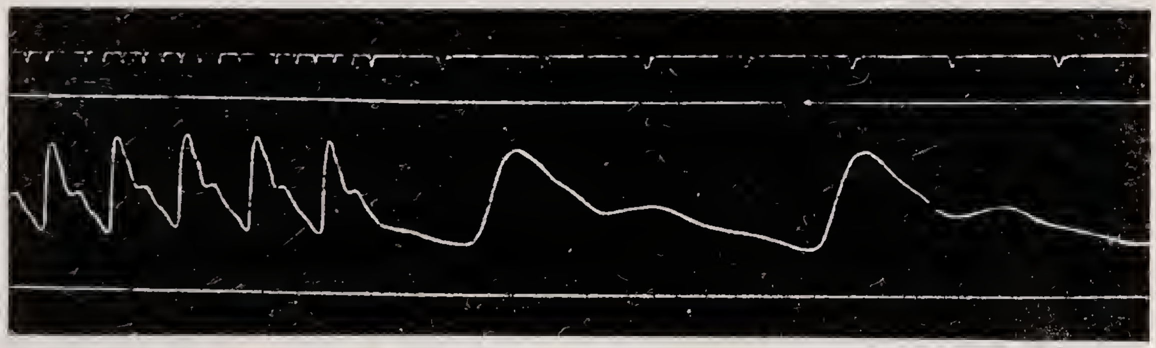


Fig. 41.—Normal pulse of healthy young man. Obvious dicrotic wave. Maximal blood pressure 120, minimal 70 mm.

of the semilunar valves since in the more peripheral arteries it may sometimes be delayed. It is, however, possible to measure accurately on the radial curve the systolic interval from the beginning of the ascending limb to the beginning of the dicrotic notch, and from this point onward the diastolic interval. The dicrotic notch is deeper if the pulse is soft, so deep that the pulse wave may be palpably interrupted. Such a pulse is spoken of as **dicrotic.** Dicrotism usually appears in fever and its development may be recorded as the fever increases (see Figs. below).

Radial Pulse Curves

The curves illustrated below have been recorded with the sphygmograph of O. Frank and Petter. In all of them the first portion is taken at a slow speed and the second at a more rapid, so that in the second portion the curve appears to be drawn out. The time record above is written in fifths of a second (Figs. 41–46).

THE PHYSICAL SIGNS OF THE MORE IMPORTANT TYPES OF HEART DISEASE

Alterations of the valve leaflets produced by vegetations, ulcerations, thickening, adhesions or contractions may influence the circulation in either or both of two directions: In the first place complete closure of the valvular orifice may be rendered impossible (insufficiency), or secondly, due to adhesions or thickening of the valve, its orifice may be narrowed (stenosis). The effect of valvular insufficiency (and the physical signs thereof) will, therefore, be apparent in that phase of the heart cycle during which the orifice involved is normally closed, and of stenosis during the period when

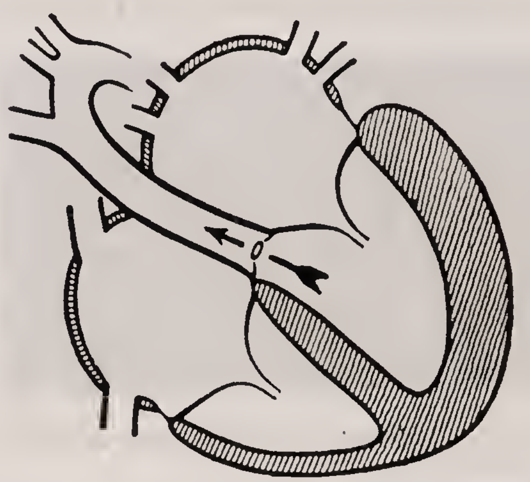


Fig. 47.—Aortic stenosis. Left ventricle hypertrophied but only slightly dilated. Systolic murmur over aortic area.

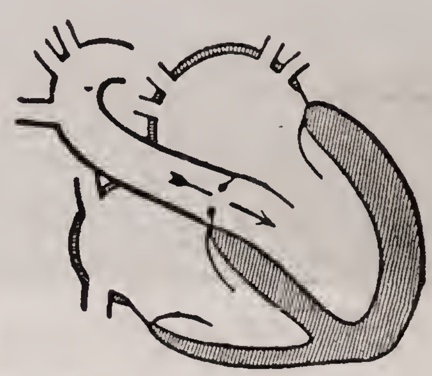


Fig. 48.—Aortic insufficiency. Left ventricle dilated and hypertrophied. Diastolic murmur at aortic area.

the valve in question is normally open and allows the blood stream to pass.

Aortic stenosis is produced by an inflammatory change in the valvular endocardium such that the leaflets are thickened and adherent at their free margins. Narrowing of the aortic orifice produces obstruction to the outflow of blood from the left ventricle so that this chamber hypertrophies and dilates. The cardiac impulse is circumscribed, rather more to the left than normal, and sometimes heaving. The relative cardiac dulness is moderately enlarged to the left. With increasing stenosis, or insufficiency of the left ventricle, the relative cardiac dulness is conspicuously increased to the left, and the cardiac impulse is abnormally far to the left and heaving. A loud systolic murmur, accompanied often by a

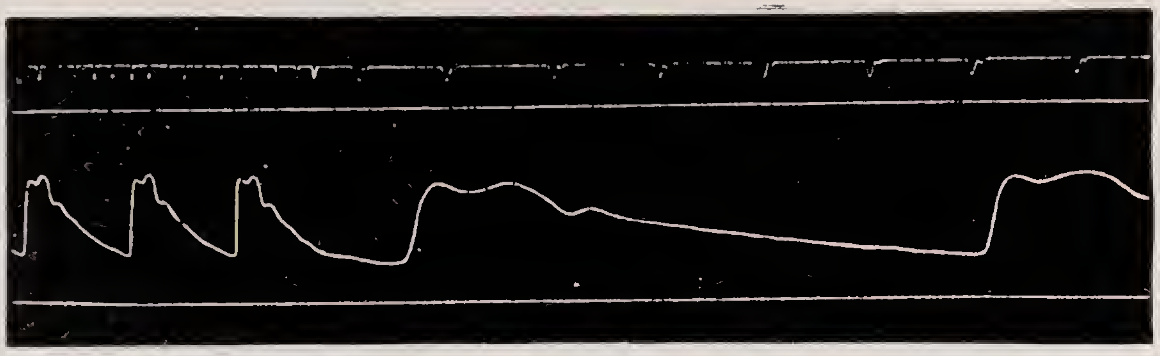


FIG. 42.—Pulse in hypertension with nephritis. Anacrotic wave marked, dicrotic wave less pronounced. Maximal blood pressure 200, minimal 140 mm.

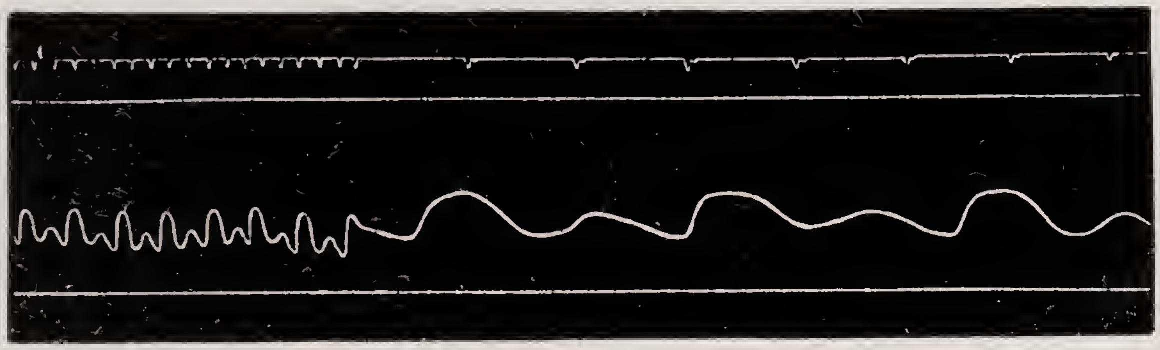


FIG. 43.—Complete dicrotic pulse in sepsis. Systolic peak rounded, anacrotic wave absent. Dicrotic notch very sharp. Maximal blood pressure 80, minimal 50 mm.

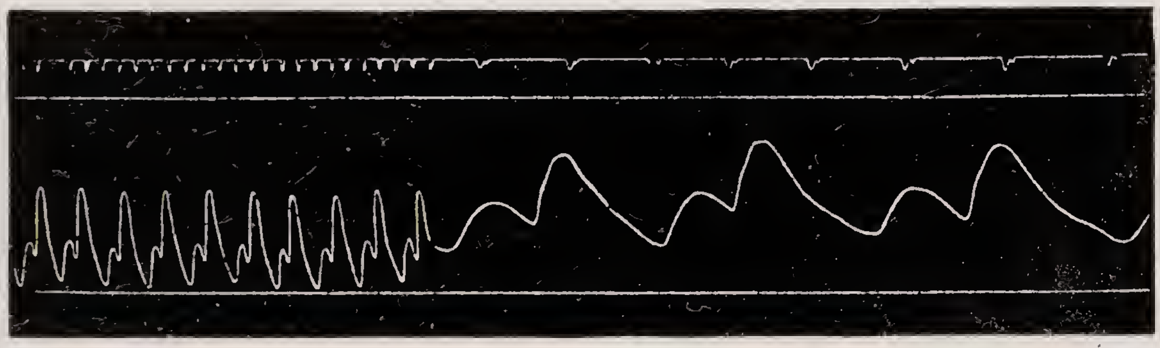


FIG. 44.—Pulse in sepsis with high fever. Chief systolic wave begins before dicrotic wave of preceding pulse has subsided. Maximal blood pressure 100, minimal 50 mm.

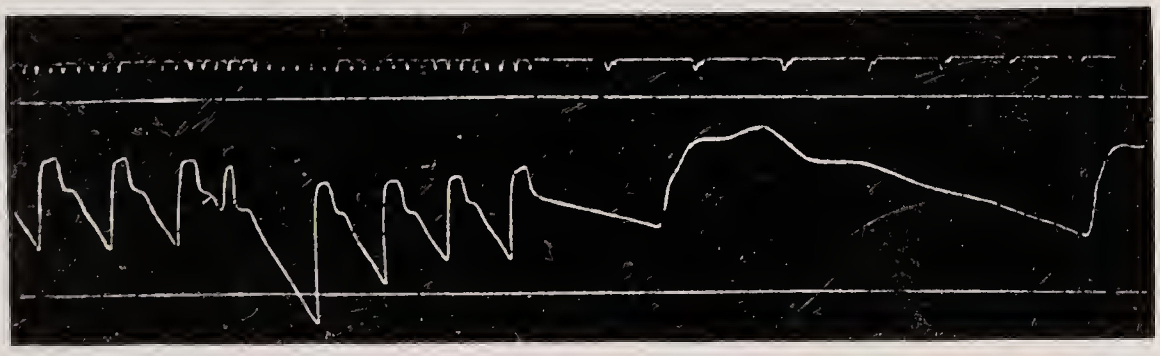


FIG. 45.—Pulsus tardus with aortic stenosis. There is a notch in the ascending limb; the accessory systolic wave rises above the chief wave. At X an extrasystole and compensatory pause. Maximal blood pressure 110, minimal 80 mm.

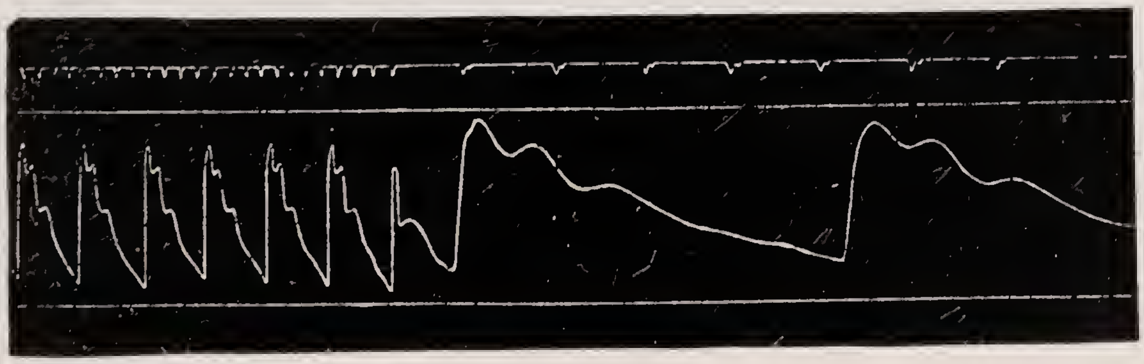


FIG. 46.—Bounding pulse with aortic insufficiency. Maximal blood pressure 130, minimal abnormally low, 40 mm.

usually enlarged to the left and upward (particularly in the third left intercostal space), and to the right. Enlargement of the relative cardiac dulness to the right may be taken to indicate that not only the right ventricle but also the right auricle is dilated as a result of stasis in the pulmonary circulation. Just to the left of the sternum and in the epigastrium the forceful pulsation of the hypertrophied right ventricle may be palpable. A diastolic, low-pitched murmur, usually with a late diastolic accentuation (crescendo murmur), audible at and just within the apex, usually ending with accentuated first mitral sound. Second pulmonic sound accentuated, due to forcible closure of the valves by the in-

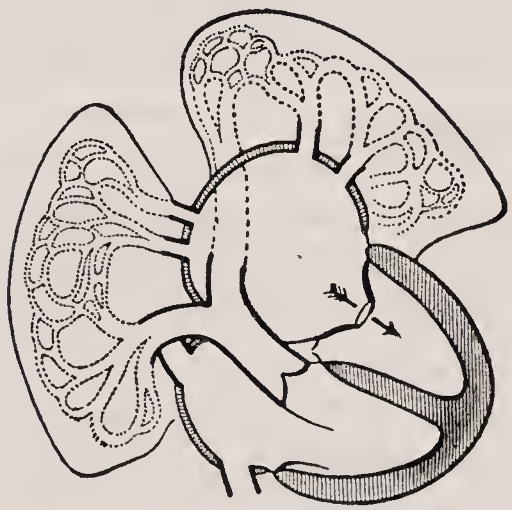


Fig. 49.—Mitral stenosis. Left auricle dilated, right ventricle hypertrophied, pulmonary artery dilated. Pulmonary circulation overfilled. Diastolic murmur at the mitral area.

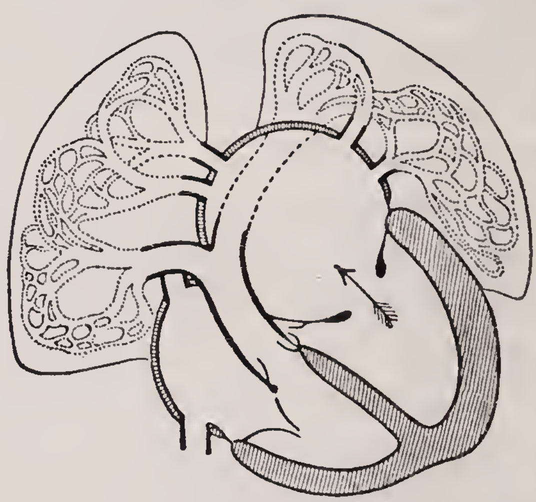


Fig. 50.—Mitral insufficiency. Left ventricle dilated and hypertrophied. Left auricle dilated, right ventricle hypertrophied. Pulmonary artery dilated, pulmonary circulation overfilled. Systolic murmur at the mitral area.

creased pressure in the lesser circulation. The second sound may often be reduplicated. Pulse small and soft.

Mitral insufficiency is produced by warty vegetations, by ulcerations on, or by cicatricial thickening and shortening of, the mitral leaflets and their chordæ tendineæ. A portion of the contents of the left ventricle is driven back into the left auricle during systole; the auricle becomes overfilled and stasis in the pulmonary circulation with resultant hypertrophy of the right ventricle and accentuation of the second pulmonic sound result. Dilatation of the right ventricle and auricle follows, with enlargement of the relative cardiac dulness to the right and upward, when the right ventricle is no longer able to overcome the congestion in the lesser circula-

tion. The overfilled left auricle discharges an abnormally large amount of blood into the left ventricle which in turn becomes overfilled, dilated and sometimes hypertrophied. Cardiac impulse forceful and diffuse particularly to the right; relative cardiac dulness enlarged to the left and usually upward. A systolic murmur at and near the apex transmitted into the axilla, systolic murmur often also audible over the pulmonic area. First sound in the mitral area occasionally absent, second pulmonic sound accentuated. The pulse is usually normal, occasionally of increased amplitude as long as compensation is maintained; with myocardial insufficiency it becomes small and frequently irregular. If mitral insufficiency and stenosis occur together the characteristic systolic and diastolic murmurs may both be audible; the first sound may then be diminished in intensity and not, as in pure mitral stenosis, accentuated.

Tricuspid insufficiency most commonly occurs as relative insufficiency in association with disease of the mitral valve, since in the presence of extreme dilatation of the right ventricle and its auriculo-ventricular orifice the tricuspid valves are unable to close this aperture completely. With each systole there occurs a retrograde wave of blood from the right ventricle through the tricuspid orifice into the right auricle and thence into the superior and inferior venæ cavæ and their contributories. This is visible as a systolic pulsation in the jugular vein synchronous with the carotid wave. At the same time the liver pulsates with systole. The overfilling of the right auricle with consequent dilatation brings about a conspicuous enlargement of the relative cardiac dulness to the right. There appears also a systolic murmur in the tricuspid area. On account of the regurgitation of blood from the right ventricle into the right auricle the pressure in the pulmonary artery is not particularly raised and the second pulmonic sound is not accentuated. Pulse small.

Pulmonic stenosis occurs rarely, is usually congenital and often associated with other cardiac anomalies. Relative cardiac dulness usually but little enlarged. Profound cyanosis, hypertrophy of the right ventricle, systolic murmur over the

pulmonic area, faint second pulmonic sound. Pulse small.

Pulmonic insufficiency: extreme enlargement of the relative cardiac dulness to the right, pulsation in the epigastrium at about the lower end of the sternum, diastolic murmur over the pulmonic area. Pulse small.

Aneurysm of the aorta. There is usually a visible pulsation and an area of dulness in the second or third right interspace, but these signs may be absent if the aneurysm involve, not the ascending, but the arch or the descending aorta, i.e. if it lie farther posteriorly and be covered with lung. The pulsation may be transmitted to the trachea and larynx and may be palpated at the thyroid cartilage (tracheal tug). Frequently a systolic murmur in the region of the aneurysm. Cardiac hypertrophy and diastolic murmur in the aortic area appear only when there is a coincident insufficiency of the aortic valve. Sometimes the radial pulses are unequal in volume or, more rarely, asynchronous. Occasionally there may be left-sided paralysis of the recurrent laryngeal nerve and this may be the first symptom of a developing aneurysm. Upon transillumination of the chest with the X-ray there is brought into view a round, more or less localized, protrusion in the shadow of the great vessels. The pulsations of such an aneurysmal shadow are usually, although not always, visible.

Diseases of the myocardium. These may occur following infectious diseases, e.g. polyarthritis (rheumatic fever) diphtheria or syphilis, or following the abuse of alcohol or tobacco. They are evidenced by signs of a disturbed circulation. The relative cardiac dulness is usually, but not always, enlarged due to dilatation of the ventricles; the pulse is small and may be either accelerated or retarded in rate. Apex impulse is displaced outward, frequently increased in force, more rarely of lessened intensity. Heart sounds impure, frequently a functional systolic murmur in the mitral area. Signs of myocardial insufficiency and congestive failure: Dyspnœa, enlargement of the liver, albuminuria and œdema. Exactly the same signs and symptoms may occur when a previously hypertrophic myocardium (with nephritis or arteriolarsclerosis) gives way before its increased load. Myocardial insufficiency is not necessarily associated with

demonstrable anatomical alterations in the heart muscle but may be due to functional insufficiency of the muscle itself. To test the functional capacity of the heart one may employ various graduated amounts of exercise (hopping or running in place). With a diminished cardiac reserve there results an abnormal acceleration of pulse (above 120), which disappears only after several minutes. Dyspnœa may also ensue and may be demonstrated by directing the patient immediately following the exercise to count 20 in a loud voice; if dyspnœic he is usually compelled by shortness of breath to interrupt his counting.

With sclerosis of the branches of the coronary arteries or with partial obstruction of their orifices in the sinus of Valsalva there may occur, following exertion, exposure to cold, or overfilling of the stomach, paroxysmal attacks of a feeling of pressure in the region of the heart associated with extreme anxiety, or of pain arising in the præcordium and radiating into the left shoulder and down the left arm.

Under the term **angina pectoris** are described attacks of severe pain arising in the præcordium, radiating into the arms and into the carotid region, and often accompanied by fear of death. They occur especially with exertion, e.g., while getting up, and force the patient to rest; they are sometimes precipitated by cold or by a heavy meal. Such attacks are often accompanied by a temporary rise in blood pressure. Nitroglycerin or amylnitrite usually affords relief. Death may occur during an attack. At autopsy sclerosis or constriction of the coronary arteries at their junction with the aorta is sometimes (but not always) discovered.

(Similar, usually more protracted, attacks of pain occur with coronary occlusion (thrombosis). The resultant infarction of the myocardium frequently leads to acute dilatation of the ventricle with cardiac failure, and, if the patient survives, is almost always followed by mild fever and leucocytosis. In some cases a mural thrombus may form at the site of the myocardial infarct; portions of this thrombus may be carried as emboli to the lungs. Ed.)

Pericarditis. Inflammation of the pericardium may bring about a deposit of fibrin upon the serous membrane and therewith an audible friction rub (dry pericarditis), or an

effusion into the pericardial sac (exudative pericarditis). With the latter condition the relative cardiac dulness is conspicuously enlarged upward and to the right so as to assume the form of an equilateral triangle with the apex upward. The apex of the heart is surrounded by fluid and its impulse is only demonstrable with the patient bent forward; it may then be found well within the outer border of cardiac dulness. Pulse small, soft and rapid. With adhesions between the visceral and parietal pericardium (obliterative pericarditis) there often occur, but not always, a systolic retraction in the region of the heart with a rebound of the chest wall with diastole, sometimes diastolic venous collapse in the neck and usually congestion in the systemic circulation with enlargement of the liver, sometimes of the spleen, and ascites, because the heart as a result of its connective tissue sheath can neither dilate sufficiently during diastole nor contract adequately in systole.

CHAPTER IV

THE BLOOD[1]

THE total blood volume of the healthy adult, as estimated by the latest methods, amounts to about 5–6 liters (of which 3–4 liters are represented by the plasma), i.e. approximately 10% of the body weight. It is subject, in the absence of disease, to certain variations; if water be withheld the water content and therewith the total volume of blood may sink to 5 liters (2.5 liters plasma) or following the administration of large quantities of fluid and salt the blood volume may reach 9 liters (6 liters plasma). In the first case on account of the reduced plasma volume the red blood corpuscles are relatively increased in number (per cu. mm.); in the second with the increase in plasma volume the red blood cell count falls. The various procedures employed in determining the blood volume in the human body are too involved to be recounted fully here. Suffice it to say that it is incorrect to conclude from mere pallor or hyperæmia of the skin that a reduction (oligæmia) or an increase (plethora) of the blood volume is present.

REACTION OF THE BLOOD

The **reaction** of a solution is determined by the relative concentrations of H^+ and OH^- ions therein. An excess of H^+ ions, resulting from the dissociation of an acid, e.g. hydrochloric acid, which splits into kation (H^+) and anion (Cl^-), produces an acid reaction. Conversely the reaction is alkaline if the solution contain a base, e.g. sodium hydroxide which dissociates into OH^- anion and Na^+ kation. If the H^+ and

[1] In this chapter some methods of examination are described which are scarcely possible in general practice. Their performance presupposes a practical training in chemistry, particularly in microanalysis, and they can only be carried out in a well-equipped laboratory. Such procedures are briefly outlined here for the reason that they are sometimes necessary to the establishment of an exact diagnosis, and their results are frequently mentioned in case reports. The brief descriptions in this book will suffice for the expert, and, at the same time, give to the beginner an idea of the principles involved.

OH^- ions be equal in number the reaction is neutral. The ideal example of a neutral solution is pure distilled water in which the concentration of H^+ and also of OH^- ions is about $\frac{1}{10,000,000}$ gm.-ion per liter, or as it may be expressed, $\frac{1}{10^7}$, or 10^{-7}. The product of the concentrations of H^+ and OH^- ions in pure distilled water is therefore 10^{-14}. According to the law of mass action this product has the same value in every solution.

It is customary to express the hydrogen ion concentration in powers of 10, and for the sake of simplicity to write only the exponents, for which the abbreviation pH is employed. pH indicates, therefore, the negative exponent of a power of 10. The greater the denominator of the fraction, i.e. the less the value of the same and therewith the H-ion concentration and the degree of acidity, the greater will be the negative exponent of 10.

At neutrality, as suggested above, pH equals 7, and the negative exponent expressing the OH^- concentration, pOH is also 7. Between the two ions there exists always a mathematical relationship such that the **sum** of pH and pOH is always 14. The reaction of any solution may, therefore, be defined whenever the hydrogen ion concentration is stated. With an acid reaction the H^+ ions preponderate and pH is therefore less than 7; conversely with an alkaline reaction OH^- ions are in the majority and pH is greater than 7. A tenth normal solution of HCl has a pH of about 1, that is it contains 10^{-1} gm. hydrogen and 10^{-13} gm. hydroxyl ions per liter. The pH of a tenth normal sodium hydroxide solution is, on the other hand, 13 and its hydroxyl ion concentration 10^{-1} (pOH = 1.091).[1]

The hydrogen ion concentration may be measured in several ways. In biology two methods have proven most useful: (1) Electrometric determination by means of the hydrogen electrode, and (2) the indicator method. The electrometric method is the more accurate and depends in principle upon the development of a potential difference between the solution under examination and a platinum electrode satu-

[1] Slight discrepancies between measured and calculated acidity are to be explained upon the assumption of a change in ionic activity.

rated with hydrogen gas. This potential difference varies with the pH of the surrounding fluid. Less complicated is the indicator method which is based upon the properties of different dyes to change color at a certain reaction.

pH Range	Indicator	Color changes from acid to alkaline
Acid:		
1.2–2.8	Thymol blue	Red to yellow
2.9–4.0	Dimethylamino azolbenzol	Red to yellow
3.0–4.6	Bromphenol blue	Yellow to blue
3.5–5.0	Congo red	Blue to red
4.4–6.0	Methyl red	Red to yellow
4.5–8.2	Litmus	Red to blue
5.2–6.8	Bromcresol purple	Yellow to purple
6.0–7.6	Bromthymol blue	Yellow to blue
Neutral:		
6.8–8.4	Phenol red	Yellow to red
7.2–8.8	Cresol red	Yellow to red
Strongly alkaline:		
8.0– 9.6	Thymol blue	Yellow to blue
8.3–10.0	Phenolphthalein	Colorless to red

Lackmoid, which is commonly employed (in Europe) for the determination of the reaction of the urine shows the following changes:

Below pH^4	pH^5	pH^6	pH^7	pH^8
Pink	Violet	Violet-blue	Bluish violet	Blue

The reaction of the various body fluids lies, with the exception of the gastric juice and the urine (both strongly acid), in the neighborhood of neutrality. The normal pH values are as follows:

Gastric juice	0.92–1.58
Urine	5.3 –6.0
Bile	5.4 –5.5
Saliva	6.9
Blood	7.28–7.41
Cerebrospinal fluid	7.4 –7.6
Tissue fluid	7.35

The concentrations of H^+ and OH^- ions in a fluid is of particular physiological importance since certain processes

are dependent upon a definite reaction. Thus the digestive enzymes contained in gastric and pancreatic secretions are active only at a certain pH; the combination and dissociation of oxygen and hæmoglobin is closely linked with the reaction of the blood, and the regulation of respiration is for the most part a function of blood acidity, i.e. its content of carbonic and other acids which stimulate the respiratory center. The physical properties of the proteins, their stability in solution, their ability to function now as acids and now as bases, change with the pH. The maintenance of a definite reaction is obviously, therefore, of the **utmost** importance to life.

The reaction of the blood and tissue fluids is maintained with extraordinary constancy slightly on the alkaline side of neutrality. In spite of the fact that, in the course of metabolism, both organic and inorganic acids are formed and are thrown into the blood, and that both acids and bases, which might alter the reaction of the blood, are ingested with the food, the blood pH remains persistently within the limits stated above. The maintenance of this acid-base equilibrium is accomplished in several ways: If considerable quantities of acid are formed in metabolism, e.g. lactic acid during vigorous exercise, or oxybutyric or diacetic acids in diabetes, or if acid or alkali is absorbed with the food, the non-volatile acids and bases are excreted through the kidneys, and the volatile carbonic acid leaves the blood through the lungs. Furthermore the blood and tissue fluids contain certain substances which act to prevent sudden changes in reaction. To these **"buffer substances"** belong, among others, the salts of phosphoric and carbonic acids. If, for example, diacid (NaH_2PO_4), and dibasic (Na_2HPO_4) sodium phosphate be present together in a solution the addition of acid or base brings about simply a shift in the relative proportions of these salts without a change in reaction. The proteins themselves and their salts also serve as buffers in that they may function either as acids or as bases. The principal buffer is hæmoglobin; oxyhæmoglobin is a far stronger acid than reduced hæmoglobin. As suggested above the salts of carbonic acid are of particular importance to the maintenance of the reaction: From sodium bicarbonate a portion of the sodium combines with any acid radical which is added and a corresponding amount of car-

bonic acid is liberated. This passes at once into simple physical solution in the blood and is eliminated through the lungs. The proportion of dissolved CO_2 to bicarbonate is a fundamental factor in the regulation of the hydrogen ion concentration of the blood; normally $\frac{CO_2}{NaHCO_3} = \frac{1}{20}$ in the arterial blood. Although, under normal conditions, the absolute content of $NaHCO_3$ varies considerably the proportion of $\frac{CO_2}{NaHCO_3}$ remains substantially unchanged since any increase in the dissolved CO_2 is rapidly followed by an increased output through the lungs. The gaseous exchange between blood and air in the lungs follows the laws of gas absorption; the CO_2 tension in the alveolar air is, therefore, the same as that in the blood leaving the lungs, i.e. the systemic arterial blood. This amounts normally to a tension of 40 mm. Hg., or to about 3 c.c. CO_2 per 100 c.c. blood.

If, in the course of metabolism or digestion, considerable quantities of acid enter the blood, these combine with a portion of the sodium otherwise combined with carbonic acid. Less carbonic acid may, therefore, be bound. Elimination of the resultant excess of dissolved CO_2 is accomplished by increased pulmonary ventilation and the carbon dioxide tension in the alveolar air and in the arterial blood is correspondingly reduced. The proportion $\frac{CO_2}{NaHCO_3}$ and, with it, the pH remain unaltered. If, on the other hand, excessive amounts of acid enter the blood, e.g. in diabetic coma, the available supply of alkali may be so depleted that the CO_2 thus freed cannot be adequately eliminated and acidosis results.

If, on the other hand, the **blood bases,** e.g. sodium, be abnormally increased, a larger part of the carbonic acid is bound to these alkalies at the cost of the dissolved CO_2. Such an **alkalosis** may be produced by forced breathing due to the excessive removal of dissolved CO_2 from the blood: The reaction of the blood shifts in consequence, toward the alkaline side. This is characterized by increased irritability on the part of the peripheral nerves to mechanical and electrical

stimuli (**Trousseau's and Chvostek's signs**) and by tetanic cramps in the extremities and face (**tetany**).

The base available for combination with CO_2 is known as the **alkali reserve**; with alkalosis it is increased and with acidosis decreased. It may be determined by mixing freshly drawn **arterial** blood with an excess of lactic acid and evacuating the container. The bound CO_2 is thereby set free and may then be measured volumetrically or manometrically. The content of $NaHCO_3$ is proportional to the number of c.c. CO_2 which can be driven off from 100 c.c. of blood by the addition of a strong acid. This amounts normally to about 50 c.c.; in acidosis less, about 25 c.c.; in alkalosis more, i.e. 75 c.c. (By Van Slyke's technique values as low as 15 volume per cent. are sometimes obtained in diabetic coma. Ed.)

Since by this method there is measured not only the CO_2 combined with base but also that in simple physical solution, the dissolved CO_2 must be subtracted from the value so obtained. Its volume may be measured by analysis of the alveolar air. The examination of the arterial blood meets, therefore, with certain difficulties since such blood is to be obtained only by arterial puncture, e.g. radial or femoral. Venous blood may be withdrawn far more easily. But, since the CO_2 content of venous blood is extremely variable and is strikingly influenced by the degree of rest or activity on the part of the muscles in the domain of the vein in question, the alkali reserve in venous blood can only be measured by first shaking with gas mixtures of various CO_2 content, adding lactic acid, and determining how much CO_2 may be taken up by the blood at a given tension. (Van Slyke.) A curve is thus obtained from which there may be calculated the CO_2 capacity of the arterial blood.

THE RESISTANCE OF THE RED BLOOD CORPUSCLES

It has been observed in a variety of pathological conditions that the resistance of the red blood corpuscles to variations in temperature, to chemical or osmotic influences is abnormally reduced or increased. The determination of the osmotic resistance of the red blood corpuscles is of considerable practical value. This determination may be made either

with fresh blood to which a little sodium citrate has been added, or, if it is desired to exclude the effect of the serum, upon the corpuscles washed with physiological saline.

The procedure is as follows: There is first prepared a series of dilutions of sodium chloride varying in concentration by 0.02%. The method of Ribierre is the most simple beginning with 0.70%. Into a series of sterile test tubes is dropped from a burette successively 70, 68, 66, 64, etc. drops of such a solution down to 20 drops. From another burette distilled water is added 2, 4, 6, 8 drops, etc. so that in every tube there is the same volume of fluid representing dilutions of saline from 0.70–0.20%. A drop of the blood to be examined is added to each tube, the mixture is shaken and observed against a white background after an interval of from 20 minutes to 2 hours.

The destruction of the red blood corpuscles, i.e. hæmolysis, with the transfer of the hæmoglobin to the surrounding fluid normally begins at a concentration of sodium chloride of 0.45% and is complete by 0.34%. The resistance is described as reduced if hæmolysis take place at a higher concentration. The lowest saline concentration in which hæmolysis is demonstrable is designated as the minimum resistance. The tube in which all the red blood corpuscles are all but dissolved represents the maximum resistance. Particularly in hæmolytic jaundice there is a conspicuous reduction in the resistance of the red blood cells.

BLOOD GROUPING AND BLOOD MATCHING

In many severe forms of anæmia, particularly "secondary" anæmia, it is often necessary to transfuse the patient with the blood of a healthy person. The transfusion of animal blood is attended by great dangers. The transfusion of human blood sometimes produces alarming symptoms on the part of the recipient, i.e. emboli, infarction, jaundice, hæmaturia and collapse. These symptoms appear if there be present in the blood serum of the recipient substances which act either to dissolve (hæmolysins) or to clump (agglutinins) the cells of the donor.

This is to be avoided by the careful examination of the blood of the donor and the blood of the recipient before transfusion; it is most important to test the serum of each individual against the cells of the other. A small amount of blood is obtained from the patient and the serum is removed after defibrination; another specimen is collected in normal saline and the cells are carefully washed. Blood is collected from the donor in a similar fashion and a drop of the serum of each individual is mixed upon a cover-glass and inverted upon a concave slide with a drop of saline containing the cells of the other. The slides are then incubated from ½ to 1 hour; in the absence of clumping or hæmolysis in either mixture it is safe to proceed with the transfusion from the donor in question.

It has been shown that human beings, as regards their blood, may be divided into four groups (Jansky, 1907):

Group I. The cells of this group are agglutinated by the serum of none of the other groups, while its serum agglutinates the cells of Groups II, III, and IV. ("Universal donors.")

Group IV. The serum of this group produces no agglutination of the cells of any other group. Group IV patients are therefore "universal recipients;" they may safely be transfused with blood from any group.

Groups II and III. Here a more careful selection of donor and recipient is required. The corpuscles of II are agglutinated or hæmolysed by the serum of I and III, and those of III are destroyed by the serum of I and II.

These effects may be briefly summarized in the following table:

Cells	Serum I	Serum II	Serum III	Serum IV
I	−	−	−	−
II	+	−	+	−
III	+	+	−	−
IV	+	+	+	−

Serum	Cells I	II	III	IV
I	−	+	+	+
II	−	−	+	+
III	−	+	−	+
IV	−	−	−	−

In America the classification of Moss (1910) is more commonly employed: In this Groups I and IV of Jansky have been transposed.

Cells	Serum I	II	III	IV
I	−	+	+	+
II	−	−	+	+
III	−	+	−	+
IV	−	−	−	−

Serum	Cells I	II	III	IV
I	−	−	−	−
II	+	−	+	−
III	+	+	−	−
IV	+	+	+	−

Method: Blood is obtained from individuals known to belong to Groups II and III, the serum separated, and preserved by the addition of 1 c.c. of 5% phenol in glycerin to each 10 c.c. serum. A drop of a suspension of red cells of the blood to be tested is then mixed upon a cover-slip with an equal quantity of Group II serum, mounted on a concave slide, and allowed to stand for one hour. The procedure is repeated with Group III serum.

If agglutination occurs with both sera the cells in question belong to Group IV of Jansky (Group I Moss); if it takes place with neither the cells are Group I (Jansky) = (Group IV Moss). Agglutination by II serum without agglutination by III serum indicates cells of Group III; by III serum but not by II shows the cells to belong to Group II.

The following tests should be made in preparation for every transfusion:

Grouping of donor and recipient.
Cross-agglutination, donor's cells vs. recipient's serum and donor's serum vs. recipient's cells.
Wassermann reaction of donor.

Sedimentation velocity of the red blood corpuscles.

If a small amount of blood be withdrawn without stasis from a fasting patient and prevented from clotting by the addition of potassium oxalate (10 mg. to 5 c.c. blood) the red blood corpuscles gradually settle to the bottom of the tube leaving a sharp layer of clear plasma above. The sedimentation velocity is dependent principally upon the protein content of the plasma, upon the finely dispersed albumin on the one hand and the grossly dispersed globulin and fibrinogen upon the other. The larger the proportion of the latter the more rapidly and completely does sedimentation take place. In women during the menses and during gestation sedimentation takes place much more rapidly. It is also accelerated in the majority of acute febrile diseases and in exudative tuberculosis. In anæmia, diabetes and nephrosis the sedimentation is accelerated; in jaundice and in hepatic disease, retarded.

PHYSICAL PROPERTIES OF BLOOD AND SERUM

The specific gravity of whole blood varies in health between 1.045 and 1.065. It is principally dependent upon the hæmoglobin content. The specific gravity of the blood is decreased in nephritis with œdema, in the majority of anæmias, and in marasmus. To determine the specific gravity of the blood several drops are drawn from the finger into the capillary pyknometer of Schmalz and weighed upon a chemical balance.

The **specific gravity** of the **blood serum** lies normally between 1.029 and 1.031 and is dependent chiefly upon the protein content. This is reduced in hydræmia, particularly in nephritis with œdema (to 4.5%). Among the **serum proteins** the most important are albumin, and the globulins, a group which includes fibrinogen. The serum-globulin content is increased with certain types of inflammation (see sedimentation velocity). The total protein content of the serum amounts

to 6.5 to 7.5%. The dried residue of the blood serum amounts to 18 to 22%.

The **water content** of the blood is determined by weighing 5 to 10 drops of freshly drawn blood (or serum) in a weighing-glass tightly stoppered, and then repeating the process after evaporation at 65° to 70°. The water content of the blood is, on the average, 78 to 80%. It is increased (hydræmia) in anæmia, and with those forms of nephritis which are characterized by œdema.

Coagulation of the blood.

If the blood is removed from the blood vessels, e.g. by venesection, or if it is discharged into the tissues by the bursting of a blood vessel, it tends to clot within a few minutes, due to the fact that a protein, fibrinogen, present in the solution in the blood plasma, is transformed into fibrin, an insoluble fibrous mass. The clotting of fibrin is dependent upon the presence of a ferment, thrombin, which is produced from its precursor, prothrombin = thrombogen (in the blood platelets) by activation with thrombokinase. Thrombokinase is produced by the destruction of all tissue cells including the white blood corpuscles. The presence of calcium salts is indispensable to the process of clotting. If the calcium salts of the blood are thrown out of solution by means of potassium oxalate or citrate, coagulation does not take place. The clotting of the blood is delayed or decreased in many pathological conditions, e.g. in icterus (cholæmia), nephritis, and many cases of severe anæmia.

To determine the **clotting time** of the blood place a drop of physiological salt solution in a hollow-ground slide and mix therein a drop of blood freshly drawn from the ball of the finger. The slide is kept at constant temperature (25°) on a water bath. The drop is stirred with a fine glass rod. The length of time required for a thin thread of fibrin to collect on the glass rod is measured with a watch. Under normal conditions this takes place within four to five minutes. With a delay in clotting this time may be increased to ten to fifteen minutes, e.g. in jaundice and hæmorrhagic diatheses.

Somewhat more simple is the method of Lee and White: one cc. of blood is withdrawn by venapuncture into a sterile

glass syringe and placed in a clean test-tube 8 mm. in diameter. (Both syringe and test tube previously rinsed with sterile saline.) The tube is tilted every 20 seconds until surface contour remains fixed. The time required for this to take place represents the clotting time. Normal average 6–7 min. (Ed.)

Determination of the clotting time is sometimes indicated before operations inasmuch as prolonged clotting time may seriously interfere with hæmostasis.

When clotting has taken place and the clot, composed of fibrin and red blood corpuscles, has been removed, the remaining fluid is known as blood serum. It is usually transparent or slightly clouded by very small fat droplets. The color of blood serum is normally yellow. In chlorosis, idiopathic hypochronic anæmia, chronic post-hæmorrhagic anæmia, and nephritis with œdema it is strikingly pale, in pernicious anæmia brownish-yellow, and in jaundice greenish-yellow, due to the presence of bilirubin. The blood serum normally contains no blood pigment, since this is held in the red blood corpuscles. Freshly-obtained blood serum assumes a reddish discoloration from dissolved blood pigment whenever destruction of red blood corpuscles has taken place.

Hæmolysis is characterized by the dissolution of the red blood corpuscles and the discharge of their hæmoglobin content into the serum. Such hæmolysis is caused by many poisons, e.g. potassium chlorate, arseniuretted hydrogen and by certain bacterial toxins and also by quinine in patients who have or have had pernicious malaria. If an animal, e.g. a rabbit, be injected with the blood corpuscles of another species, e.g. a sheep, there develops in the course of the next 10 days, in the first animal, an hæmolytic substance which is capable of dissolving the foreign corpuscles of the second animal. This hæmolysin is, however, only potent in the presence of a complement which is usually only present in fresh blood. (See Wassermann reaction, page 328). In paroxysmal **hæmoglobinuria** which occurs in certain (frequently in syphilitic) individuals under the influence of cold there takes place a similar type of hæmolysis. There is present in the blood of such patients an hæmolysin which reacts with the complement only in the cold and which then brings

about the destruction of red blood corpuscles, the discharge of hæmoglobin into the plasma and its excretion through the urine.

[The presence of hæmolysins in the blood of such a patient may be demonstrated by the **Donath-Landsteiner reaction:** Blood is obtained by venapuncture. One portion is allowed to clot and the serum is separated by centrifugation; the remainder is citrated, the red cells are washed three times with 0.85% NaCl. A 5% suspension of red cells in 0.85 per cent NaCl is then mixed with the patient's serum. (To insure the presence of complement it is advisable to add one part in ten of fresh guinea-pig serum). The mixture is placed on ice for 5–10 minutes and then incubated at 37° C. In cases of paroxysmal hæmoglobinuria hæmolysis of the patient's cells—or of those of another patient of the same blood group —may be produced by this procedure. Ed.]

The **color** of the arterial blood is usually a bright red on account of its high content of oxygen-containing, (oxy-) hæmoglobin. The venous blood is poorer in oxygen and a correspondingly darker bluish-red. If blood be diluted with several volumes of water it shows upon spectroscopic examination the two absorption bands of **oxyhæmoglobin** in the yellow and green (between the B and E lines of Fraunhofer). If, now, a reducing substance, e.g. dilute ammonium sulphate solution be added drop by drop, the two bands of oxyhæmoglobin disappear and there appears in their place a single band characteristic of oxygen-free (reduced) hæmoglobin. The oxygen content of the arterial blood amounts normally to 21 c.c. per 100 c.c., that of the venous blood during rest to about 16 c.c. Thus in its course through the capillaries the blood loses about 5 c.c. oxygen. In severe diseases of the lungs (pneumonia) and circulatory insufficiency the oxygen content of the blood is considerably decreased.

In **poisoning with CO** the blood is a bright, cherry red and shows upon spectroscopic examination two bands which are very similar to those of oxyhæmoglobin but differ therefrom in that they lie somewhat closer together and do not disappear upon the addition of dilute ammonium sulphate.

In poisoning with potassium chlorate, analin, acetanilid,

phenacetin, etc. the blood assumes a chocolate color and shows upon spectroscopic examination, next to the bands of oxyhæmoglobin, a band in the red characteristic of methæmoglobin. The methæmoglobin band is often visible only when the blood has been diluted with water to the point at which the two oxyhæmoglobin bands no longer appear. Upon reduction with ammonium sulphate the methæmoglobin band disappears giving place to the band of reduced hæmoglobin.

A solution of methæmoglobin may be prepared by diluting normal blood with water and adding a few drops of dilute solution of potassium ferrocyanide.

The hæmoglobin content of the blood averages 16.3 gm. in men, and 14.5 gm. in women, per 100 c.c. of blood. Both the hæmoglobin content and the red blood cell count show certain individual variations depending upon the altitude at which the individual lives. In the inhabitants of certain alpine resorts, as well as in aviators accustomed to great heights, the hæmoglobin content and the number of red corpuscles is considerably higher than the average normal.

Upon heating hæmoglobin breaks down into brown hæmatin and protein. Every blood-containing fluid, therefore, contains protein and becomes brown upon boiling. If a small amount of blood (from a spot on a garment or cloth) be heated to boiling with glacial acetic and a trace of sodium chloride and cooled gradually on a slide, there form brownish-yellow rhomboid crystals of acid-hæmatin = hæmin (Teichmann's crystals). The preparation may be moistened with glycerin and examined under high magnification. The hæmin test is, however, only of value provided the blood is chemically only slightly altered.

BLOOD CHEMISTRY

In blood plasma or blood serum is a number of dissolved substances which are in part absorbed with the food, and in part represent intermediary products of metabolism (e.g. glucose). In addition are found certain salts, particularly sodium chloride, and the end-products of metabolism (urea, uric acid, creatinin, indican, etc.) which are excreted through the kidneys. The quantitative estimation of these substances in the serum is of the greatest practical importance in the

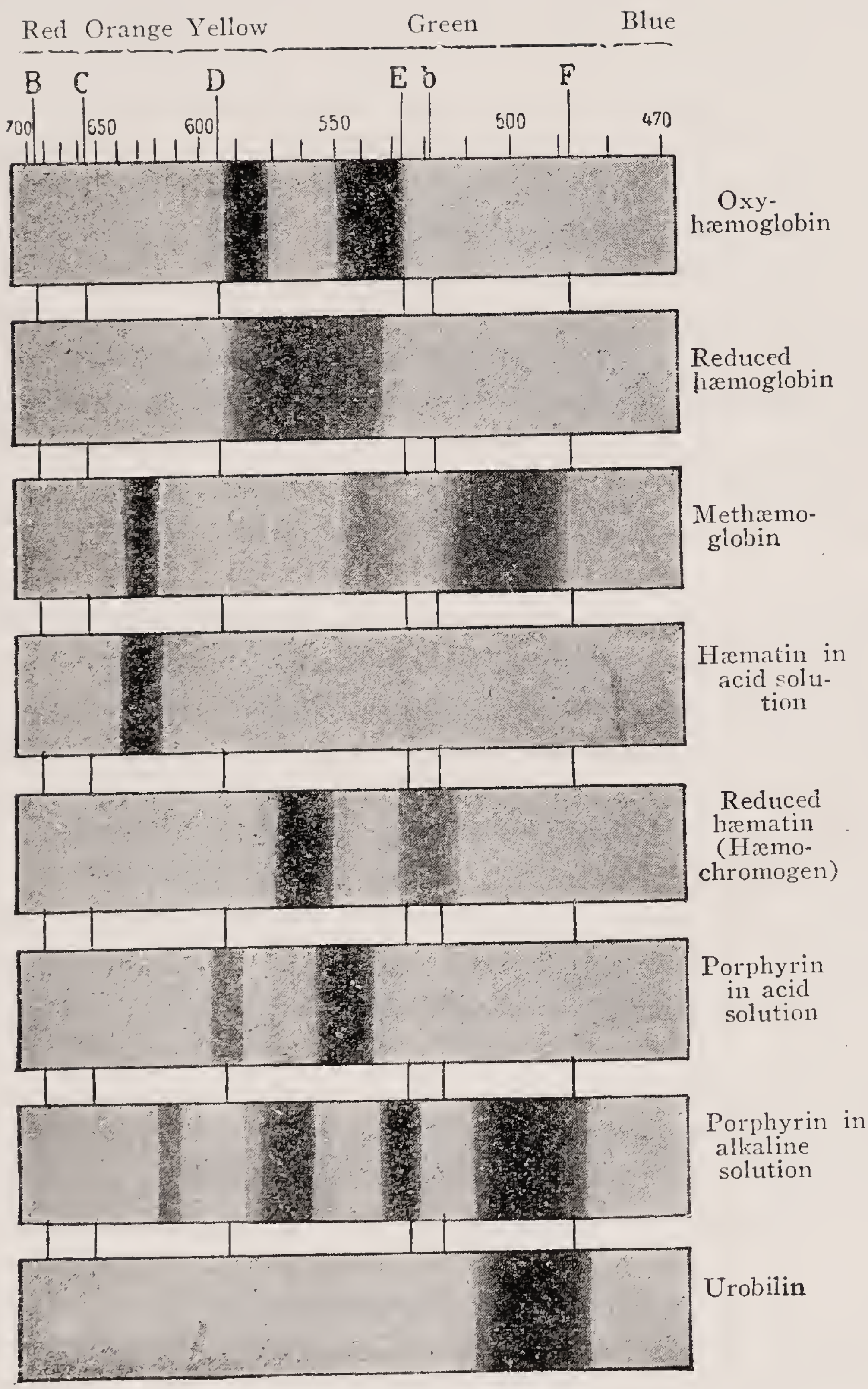


FIG. 51.—Table of spectra.

diagnosis and treatment of certain diseases (e.g. nephritis and diabetes).

Precipitation of Protein. For the quantitative estimation of these substances it is usually necessary to precipitate the proteins of the blood. This may be accomplished by the method of Neubauer in which 10 c c. of blood serum are diluted with 30 c.c. of water and then mixed with 10 c.c. of a 1.55% solution of uranyl acetate. This mixture is filtered through a dry filter; the filtrate contains the various serum constituents, other than the proteins, in a dilution of 1:5. In Folin's method 5 c.c. of oxalated blood are diluted with 35 c.c. of water and mixed with 5 c.c. of a 10% solution of sodium tungstate and 5 c.c. of 2/3 normal sulphuric acid. Several drops more of 2N sulphuric acid must usually be added to obtain an absolutely clear filtrate. Filtration is carried out by the same method and the resultant dilution is 1 :10.

Non-protein nitrogen. The nitrogen-containing end-products of protein and nuclein metabolism, are carried by the blood to the kidneys through which they are excreted. Urea makes up about 60% of these substances; the remainder is composed of ureates, creatin and indoxyl. In many forms of nephritis the excretion of these metabolic products is impaired so that they accumulate in the blood serum. This retention of the nitrogenous metabolites may be measured by the quantitative determination of the nitrogen content of the protein-free serum filtrate. Under normal conditions the non-protein nitrogen amounts to no more than 40 mg. N per 100 c.c. blood serum. With renal insufficiency it may increase to 60–100 or more mg.%. The non-protein nitrogen is determined by digesting a portion of the serum filtrate with concentrated sulphuric acid after Kjeldahl's method, distilling off the nitrogen as ammonia, and titrating it.

Reagents: I. Concentrated sulphuric acid, II. 10% copper sulphate solution, III. crystalline potassium sulphate, IV. hydrogen peroxide (C.P.), V. N/70 hydrochloric acid, VI. N/70 sodium hydroxide, VII. 33% sodium hydroxide.

Method: Ten c.c. of serum filtrate are heated in a small Kjeldahl flask over a low flame with 2 c.c. of solution I, 6 drops of solution II, and a small amount of crystalline potassium sulphate. When the fluid has become light brown in

color a drop of solution IV is added and heating continued for about 3 minutes until the mixture becomes a bluish syrup. After cooling the digestion mixture is diluted with 20 c.c. of water and connected with the distilling apparatus containing 10 to 20 c.c. of solution V. To the digestion mixture there is then added 5 c.c. of solution VII. Steam is passed through the mixture and the flask is cautiously warmed with a small burner. Distillation is continued for 8–11 minutes and the distillate is then titrated with solution VI against methyl-red to a lemon-yellow color. One c.c. of the acid corresponds to 0.2 mg. nitrogen.

Blood Chlorides (Neubauer's method). The chloride content of the blood serum ranges between 560 and 600 mg.%. In Neubauer's method the chlorides are precipitated by an excess of silver nitrate and this excess is titrated with ammonium thiocyanate against ferric ammonium sulphate as an indicator.

Reagents: I. Silver solution: to 85.5 c.c. of N/10 silver nitrate are added 30 gm. of ferric ammonium sulphate dissolved in 30 c.c. of concentrated nitric acid. The mixture is then diluted with water to 500 c.c. One c.c. of this solution corresponds to 1 mg. sodium chloride. II. Thiocyanate solution: 85.5 c.c. of N/10 solution of ammonium thiocyanate is diluted with water to 500 c.c.

Method: Six c.c. of serum filtrate are mixed in a 30 c.c. graduated cylinder with 9 c.c of solution I and diluted with distilled water up to 30 c.c. The mixture is then filtered through a dry filter into an Erlenmeyer flask and 25 c.c. of this filtrate are titrated with solution II to the point at which a brownish-red color begins to appear.

Calculation: Twenty-five c.c. of filtrate correspond to 1 c.c. of serum and 7.5 c.c of silver solution. Therefore 750–(100 × c.c. solution II) = NaCl mg.%. This product multiplied by 0.607 gives the value for chlorides alone.

Many micro-chemical methods for the estimation of the blood constituents involve the comparison of intensity of color (**colorimetry**). A solution containing a known quantity of the substance in question is usually treated in the same fashion as the serum. The resultant colors are then compared in a Dubosq or Autenrieth colorimeter; here the colors are matched by varying the depth of solution through which

light is caused to pass. In the Autenrieth colorimeter the standard solution is enclosed in a wedge-shaped glass vessel which may be raised or lowered until the color is equal to that of the solution in question. The position of the vessel may be read on a millimeter scale. The concentration of the unknown solution is calculated by the proportion $x:b = (100 - a):100$; a = scale reading, b = concentration of the standard solution, x = concentration of the unknown. This colorimeter should be calibrated with solutions of known composition. From the resultant curve it is possible to read directly from the scale the corresponding concentrations.

Uric Acid (Neubauer's method). Uric acid is present in small quantities in the blood serum of the normal person, in somewhat larger amounts following the ingestion of meat, and in smaller and more constant amounts on a purine-free diet (see chapter on metabolism). The concentration of uric acid amounts in health, upon a purine-free diet, to 2 – 3.5 mg.%. This concentration is increased to 4 – 10 mg.% commonly in gout and sometimes in those diseases which bespeak a gouty diathesis; it is sometimes raised as well in those forms of nephritis with which an increase in the non-protein nitrogen is associated, during fever, with leukæmia, carcinoma and other diseases characterized by extensive destruction of nuclear material.

Uric acid reduces phosphotungstic acid forming a blue color; the intensity of this color is proportional to the concentration of uric acid.

Reagents: I. Uric acid reagent of Folin and Trimble: 100 gm. sodium tungstate and 160 c.c of water are placed in a 500 c.c. Erlenmeyer flask, 50 c.c. of 85% phosphoric acid are added and hydrogen sulphide is passed through the mixture over night. The resultant mixture is then filtered, boiled for 1 hour with a reflux condenser, refiltered, decolorized with bromine and the excess bromine is removed by 10 minutes' boiling. In a second flask 25 gm. lithium carbonate are boiled with 50 c.c. of 85% phosphoric acid and 200 c.c. of water until all CO_2 has been driven off; this mixture is then cooled. Both solutions are mixed in a volumetric flask and diluted to 1 liter. II. Uric acid standard solution: 200 mg. of uric acid are dissolved in 50 c.c. of an 0.5% solution of

lithium carbonate and diluted to 1 liter. III. A saturated solution of sodium bicarbonate (22%).

Method: In practice the standard solution is diluted 1 :10 and the comparator vessel filled with a mixture of 1 part of solution I to 9 parts of solution III.

Two c.c. of the serum filtrate are mixed with 0.1 c.c. of solution I and 0.9 c.c. of solution III. After standing for 8 minutes the known and unknown are compared in the colorimeter.

Creatinine (Neubauer). Creatinine reduces picric acid in alkaline solution producing a brownish color (Jaffé's reaction). The intensity of the brown color is proportional to the quantity of creatinine present in solution.

Reagents: I. 1.2% solution of pure picric acid, II. normal sodium hydroxide, III. creatinine standard: 0.1 gm. of pure creatinine dissolved in 20 c.c. of 1/10 normal hydrochloric acid and diluted with water to 100 c.c.

Method: For comparison 2 c.c. of the standard solution are diluted to 100 c.c. (2 mg.%) and the vessel is filled with a mixture of 15 c.c. of solution I and 5 c.c. of solution II and 20 c.c. of the diluted standard solution.

Two c.c. of serum filtrate are mixed with 1.5 c.c. of solution I and 0.5 c.c. of solution II. Comparison made in the colorimeter after 10 minutes.

Total Creatinine. Upon heating with a mineral acid creatin is transformed into creatinine.

Reagents: As for the determination of creatinine with the addition of IV normal hydrochloric acid.

Method: The blood filtrate is heated on a water bath for 5 hours with half its volume of solution IV and, after cooling, is neutralized with half its volume of solution II. The serum filtrate is thereby diluted to double its volume and in this dilution the estimation of creatinine is carried out as above.

Blood Sugar (Hagedorn-Jensen). Reducing substances, of which glucose is the most important, are always present in the blood and normally amount to 60 to 120 mg.%. In diabetes mellitus the blood is abnormally rich in sugar (200 to 600 mg.%).

The blood sugar is determined in the total blood and not in the blood serum. The protein is thrown down with zinc hydroxide. The protein-free filtrate is mixed with an

excess of potassium ferricyanide which is reduced by glucose to potassium ferrocyanide. The excess of ferricyanide is then titrated with iodine.

Reagents: I. Zinc sulphate solution: 45 g. of zinc sulphate are dissolved in water and diluted to 100 c.c. Before using this solution is diluted 100 times. II. N/10 sodium hydroxide prepared freshly every week from N/2 sodium hydroxide. III. N/50 solution of potassium ferricyanide, 1.65 g. potassium ferricyanide and 10.6 g. of fused sodium carbonate are dissolved in a little water and diluted to 1 liter. This solution should be kept in a brown bottle. IV. Zinc sulphate-sodium chloride solution: 10 g. zinc sulphate and 50 g. sodium chloride are dissolved in water and diluted to 160 c.c. V. Potassium iodide solution: 12.5 potassium iodide are dissolved in water and diluted to 100 c.c. (Keep in a brown bottle!) Before using 40 parts of solution IV are mixed with 10 parts of solution V. This mixture should also be prepared freshly every week and should not be exposed to the light. VI. Acetic acid solution: 3 c.c. of glacial acetic diluted to 100 c.c. with water. VII. Starch solution: 1 g. of starch is dissolved with gentle heating in 5 c.c. of water and diluted to 100 c.c. with saturated sodium chloride solution. VIII. N/50 sodium thiosulphate solution: 5 c.c. of 1/10 normal thiosulphate solution, made stable by the addition of 0.053 g. of water-free sodium carbonate, is diluted to 100 c.c. IX. N/50 potassium iodate solution: 0.5566 g. potassium iodate are dissolved in water and diluted to 2 liters. This solution serves for the titration of solution VIII. For this purpose 2 c.c. of the iodate solution are mixed with 2 c.c. of solution VI, 2 c.c. of solution V and 2 drops of solution VII and titrated against solution VIII to the disappearance of the blue color. The thiosulphate solution may decompose rapidly and should, therefore, be titrated against solution VIII before each sugar determination, and the factor calculated by dividing by 2 the number of cubic centimeters of solution VIII required in the titration.

Method: The blood is drawn into a special pipette (0.1 c.c. capacity) from a small wound in the ball of the finger. The solution for precipitating the protein should be prepared beforehand: 1 part of solution II and 5 parts of the diluted solution I are mixed in each of 2 test tubes 15 mm. in diameter and 120 mm. high. There is thus formed a colloidal solution of

zinc hydroxide. Into one test tube is pipetted 0.1 c.c. of blood; the pipette is thoroughly rinsed by filling and emptying twice with the mixture. The second test tube serves as a blank. It is advisable to perform each test with two specimens and two controls.

Twenty estimations may be performed at the same time. The test tubes are heated for 3 minutes in a boiling water bath. During this process other test tubes are prepared (30 mm. in diameter and 100 mm. in length), in each of which is placed a small funnel containing a small wad of cotton wool. Through these filters the contents of the test tubes are passed, after which they are washed 3 times with 2 c.c. of water. After filtration is complete exactly 2 c.c. of solution III are added to each tube and the specimen is heated for 15 minutes on a boiling water bath. After cooling they may be allowed to stand indefinitely but up to this point the procedure must be carried out immediately after withdrawing the blood. Each specimen is now mixed with 2 c.c. of the mixture of IV and V, 2 c.c. of solution VI and 2 drops of solution VII and titrated with solution VIII to the disappearance of the blue color. From the accompanying table, given the strength of solution VIII, one may read off the glucose content of the blood per 100 c.c. from the number of c.c. of solution VIII required. One finds first the figure represented by the c.c. of VIII required in the blank determination and then that for the blood determination. The difference between the two values gives the glucose content of the blood in grams per cent:

Cholesterol (Autenrieth). The serum is saponified and the cholesterol extracted with chloroform. With acetic anhydride and sulphuric acid cholesterol produces a green color.

Reagents: I. 25% potassium hydroxide, II. Chloroform, III. Anhydrous sodium sulphate, IV. Acetic anhydride, V. Concentrated sulphuric acid, VI. Standard cholesterol solution; 100 mg. cholesterol dissolved in 100 c.c. chloroform.

Method: One c.c. serum is mixed in a small vessel with 10 c.c. of solution I and placed for 2 or 3 hours upon a boiling water bath. The mixture is then shaken in a separatory funnel with 10 c.c. of chloroform. The chloroform layer is then poured off and the aqueous remainder extracted twice with 8 c.c. chloroform. The purified extract is then washed 3 times

C. cm $\frac{M}{200}$ Thiosulphate = g glucose in 100 ccm. blood.

	0	1	2	3	4	5	6	7	8	9
0.0	0.385	0.382	0.379	0.376	0.373	0.370	0.367	0.364	0.361	0.358
0.1	0.355	0.352	0.350	0.348	0.345	0.343	0.341	0.338	0.336	0.333
0.2	0.331	0.329	0.327	0.325	0.323	0.321	0.318	0.316	0.314	0.312
0.3	0.310	0.308	0.306	0.304	0.302	0.300	0.298	0.296	0.294	0.292
0.4	0.290	0.288	0.286	0.284	0.282	0.280	0.278	0.276	0.274	0.272
0.5	0.270	0.268	0.266	0.264	0.262	0.260	0.259	0.257	0.255	0.253
0.6	0.251	0.249	0.247	0.245	0.243	0.241	0.240	0.238	0.236	0.234
0.7	0.232	0.230	0.228	0.226	0.224	0.222	0.221	0.219	0.217	0.215
0.8	0.213	0.211	0.209	0.208	0.206	0.204	0.202	0.200	0.199	0.197
0.9	0.195	0.193	0.191	0.190	0.188	0.186	0.184	0.182	0.181	0.179
1.0	0.177	0.175	0.173	0.172	0.170	0.168	0.166	0.164	0.163	0.161
1.1	0.159	0.157	0.155	0.154	0.152	0.150	0.148	0.146	0.145	0.143
1.2	0.141	0.139	0.138	0.136	0.134	0.132	0.131	0.129	0.127	0.125
1.3	0.124	0.122	0.120	0.119	0.117	0.115	0.113	0.111	0.110	0.108
1.4	0.106	0.104	0.102	0.101	0.099	0.097	0.095	0.093	0.092	0.090
1.5	0.088	0.086	0.084	0.083	0.081	0.079	0.077	0.075	0.074	0.072
1.6	0.070	0.068	0.066	0.065	0.063	0.061	0.059	0.057	0.056	0.054
1.7	0.052	0.050	0.048	0.047	0.045	0.043	0.041	0.039	0.038	0.036
1.8	0.034	0.032	0.031	0.029	0.027	0.025	0.024	0.022	0.020	0.019
1.9	0.017	0.015	0.014	0.012	0.010	0.008	0.007	0.005	0.003	0.002

with a little water, shaken with 5 gm. of anhydrous sodium sulphate and filtered through a dry filter into a 25 c.c. flask. Five c.c. of this chloroform solution are mixed with 2 c.c. of solution IV and 3 drops of solution V and allowed to stand for 15 min. in a dark place at 30°–35° C. At the same time 10 c.c. of the standard solution are mixed with 4 c.c. of solution IV and 6 drops of solution V and treated in the same fashion. The two specimens are compared in the colorimeter.

Calculation:

$$\frac{200 \times (100 - \text{colorimeter reading})}{100} = \text{mg.\% cholesterol}$$

Calcium: Normal human blood serum contains from 9–11 mg. calcium per 100 c.c. The blood calcium is low in hypoparathyroidism and rises after the injection of parathyroid extract. It is also decreased in infantile tetany and in severe nephritis.

Calcium determination in the blood serum (after **Clark**[1]).

Principle: The calcium is precipitated from the serum as oxalate, redisolved by means of sulphuric acid and titrated with permanganate. Solutions: I 5% ammonium chloride, II 3% ammonium oxalate, III N/100 potassium permanganate, IV normal sulphuric acid, V 3% ammonia.

Method: 2 c.c. serum are mixed with 3 c.c. water, 1 c.c. solution I, and 3 c.c. solution II in a centrifuge tube and allowed to stand for at least 3 hours, preferably over night. Then it is centrifuged 20 minutes, the supernatant fluid is carefully drawn off, and the precipitate washed 3 times with 3 c.c. solution V and centrifuged. The precipitate is dissolved in 5 c.c. solution IV, heated one minute in a boiling water bath and immediately titrated with solution III. The end point is marked by the appearance of a pink color which persists for one minute. Calcium determinations should always be carried out in duplicate.

Calculation: Mg.% calcium = 10x

in which x equals c.c. N/100 permanganate required. (From x subtract the blank—that quantity of permanganate required to titrate 2 c.c. of solution IV to required end point.)

Serum Bilirubin (Van den Bergh reaction). The diazoreaction of Ehrlich is applied to the serum. A red color (azobilirubin) is developed upon the addition of an acid solution of a diazonium salt to a solution containing bilirubin.

Collection of blood: Blood serum or plasma are equally suitable. As it is difficult to avoid hæmolysis when blood is allowed to clot, plasma is most convenient, using 0.2 c.c. of a 10% solution of potassium oxalate (evaporated to dryness) for 10 c.c. of blood as anticoagulant. The blood must be fresh as the bilirubin oxidizes on standing and the quality of the reaction may change. Test tubes and pipettes used must be perfectly clean.

Reagents: Solution A. Sulphanilic acid 0.1 gr., concentrated HCl 1.5 c.c., distilled water 100 c.c. Solution B. Sodium nitrite 0.5 gm., distilled water 100 c.c. Both solutions should be freshly prepared every 15 days. Before the test 5 c.c. of solution A are mixed with 0.15 c.c. of solution B.

Qualitative reaction: One c.c. of oxalated plasma (or

[1] Clark: Journ. Biol. Chem. 1921, **49**, 487.

serum) is placed in a small test tube and 0.5 c.c. of the diazo-reagent added. The appearance and development of the color reaction is watched and timed.

Direct reaction: The mixture becomes red immediately.

Biphasic reaction: The color reaction appears at once as in the first type, or within 30 seconds, but its **maximum intensity** is reached after a variable time. If the color reaches its maximum intensity quite rapidly the reaction is called "prompt biphasic" while it is called "delayed biphasic" when the color deepens quite slowly.

Indirect reaction: The color reaction first appears one or more minutes after the addition of the reagent. The maximum intensity is reached only after a considerable period or upon the addition of alcohol.

Quantitative determination: Standard; a solution of cobaltous sulphate. If dried anhydrous cobaltous sulphate is used, take 21.610 gm. in 1000 c.c. of distilled water. If crystallized cobaltous sulphate is used, ($CoSO_4 \cdot 7H_2O$), take 39.150 gm. in 1000 c.c. of distilled water. This standard is taken by Van den Bergh as equal to 1 unit, and corresponds to $\frac{1}{200{,}000}$ bilirubin, i.e. 0.5 mg.%.

Serum or plasma giving indirect reaction. One c.c. of serum and 2 c.c. of alcohol (96%) are shaken and centrifuged. One c.c. of the supernatant fluid is placed in a test tube with 0.25 c.c. of reagent and 0.5 c.c. of alcohol are added. The color is compared with the standard in any microcolorimeter. The first dilution, as a result of the contraction due to alcohol, is $\frac{20}{7}$. The second dilution is $\frac{7}{4}$. The final dilutions will be

$\frac{20}{7} \times \frac{7}{5} = \frac{1}{4}$ Therefore,

$$\frac{\text{Reading of standard}}{\text{Reading of unknown}} \times 5 = \frac{\text{units}}{2} = \text{mg. bilirubin per cent.}$$

Serum giving biphasic reaction or low bilirubin content with direct reaction. Thanhausen and Andersen's modification is recommended: To 1 c.c. of plasma or serum are added 0.5 c.c. of reagent. (Shake well.) One or two minutes later 2.5 c.c. alcohol (96%) and 1 c.c. of a saturated solution of

$(NH_4)_2SO_4$ are added and the mixture is shaken and centrifuged. Calculation:

$$\frac{\text{Reading of standard}}{\text{Reading of unknown}} \times 4 = \frac{\text{units}}{2} = \text{mg. bilirubin per cent.}$$

(If the color of the unknown is too strong, dilute with 2 parts of alcohol and 1 part of water.)

Serum having high bilirubin content (direct reaction). Five-tenths c.c. of plasma or serum are mixed with 0.5 c.c. reagent. Water is added (varying measured quantities to get a reasonable dilution) and then alcohol, so that the fluid is increased to thrice its volume. The preparation is then centrifuged and compared in the colorimeter with the standard. **Calculaticn:**

$$\frac{\text{Reading of standard}}{\text{Reading of unknown}} \times \text{dilution} = \frac{\text{units}}{2} = \text{mg. bilirubin per cent.}$$

[Barron, (Trans. Assn. Am. Physicians, 1929), has demonstrated that the direct reaction occurs whenever bile salts are present in the blood. This property is not unique to the bile salts but is observed whenever any surface-active substance (sodium oleate, alcohol, chloroform, acetone, etc.) is added to the serum. The significance and interpretation of the **indirect reaction** is, therefore, evident. As the bilirubin, formed within the group of cells constituting the reticulo-endothelial system, is poured out into the blood stream it is adsorbed by the serum. This adsorption prevents the bilirubin from being excreted through the kidneys and from being rapidly oxidized, properties characteristic of the indirect type of bilirubin. In pathological conditions this reaction will, therefore, be found whenever increased red-cell destruction is associated with inability on the part of the liver cells to excrete bilirubin.

The **direct reaction,** on the contrary, will be found whenever surface-active substances are poured into the blood stream, which, by their strong affinity to the protein prevent bilirubin adsorption and set this pigment free in the colloidal system. Obviously this is the case in obstructive jaundice in which the bile salts formed in the liver cells are poured into the blood.

In conclusion, the serum bilirubin giving the direct and indirect reactions is identical. In the indirect reaction bilirubin is adsorbed in the serum probably by the proteins, while in the direct type this adsorption is prevented by the presence of

strongly surface-active substances which, being adsorbed by the protein surface, leave the bilirubin in a free condition. Ed.]

Icterus Index: Principle: The intensity of the yellow color of the serum is compared with that of a standard solution of potassium bichromate.

Reagents: I. Potassium bichromate 0.01% to which have been added 2 drops of concentrated sulphuric acid per 500 c.c. II. Sodium chloride solution 0.9%.

Procedure: Separate the serum from 4 or 5 c.c. of freshly drawn unhemolyzed blood. According to its depth of color, dilute 1 c.c. with 0.9 per cent sodium chloride in a graduated cylinder until an approximate match with the standard potassium bichromate solution is obtained. Compare these solutions in a colorimeter.

Calculation:

$$\frac{\text{Reading of standard}}{\text{Reading of unknown}} \times \text{dilution} = \text{Icterus index.}$$

Murphy* has suggested a modification of the above utilizing a series of standard dilutions of the bichromate solution. The dilutions are made from a 1:100 solution of potassium bichromate to correspond with icterus index figures as follows:

Dilution	Corresponding Icterus Index	Dilution	Corresponding Icterus Index
1:10,000	1	1:500	20
1: 5,000	2	1:400	25
1: 2,000	5	1:200	50
1: 1,000	10	1:133	75
1: 666	15	1:100	100

The solutions so prepared are kept in small test tubes 10 mm. in diameter. One or two cubic centimeters of the serum to be tested is pipetted into a similar test tube, which is placed between two of the standard colors in a comparator. The figure corresponding to the dilution which matches the serum is the icterus index of the serum. Readings between those of the standards may be estimated.

Normal icterus index 4 to 6, that of latent jaundice 7 to 16, of clinical jaundice 17 and above.

In America the **Folin-Wu system**[1] is commonly employed. By this method non-protein nitrogen, urea, uric acid, creatin

* Murphy, W. P.: Arch. Int. Med., 1926, **37**, 797.

[1] For further details of methods see Hawk & Bergein, "Practical Physiological Chemistry," and Cole, "Practical Physiological Chemistry."

and creatinine, sugar, amino-acids and chlorides may be determined upon a single specimen after precipitation of the protein.

Preparation of protein-free filtrate. The blood proteins are precipitated with tungstic acid (sodium tungstate and sulphuric acid).

Method: 10 c.c. blood obtained by venapuncture are mixed with 20 mg. sodium or potassium oxalate upon removal. A measured amount of blood is then laked in a flask with 7 volumes of water and mixed with one volume of 10% sodium tungstate solution. One volume of $^2/_3$ normal sulphuric acid is then added, drop by drop, while the mixture is thoroughly shaken. Upon standing for 5–10 minutes the color of this mixture gradually changes from red to dark brown, provided coagulation is complete. If this does not occur 10% sulphuric acid should be added a drop at a time (with shaking) until the dark brown color appears. The mixture is then filtered and all determinations made upon the filtrate.

Non-protein nitrogen (Folin-Wu method): A portion of the filtrate is digested with a phosphoric-sulphuric acid mixture by a micro-Kjeldahl method and the ammonia formed is determined colorimetrically after addition of Nessler's reagent (mercury potassium double iodide).

Reagents: I. Acid mixture: 50 c.c. of 5% copper sulphate solution are mixed with 300 c.c. of 85% phosphoric acid, and 100 c.c. of ammonia-free concentrated sulphuric acid are added and mixed. Before using this mixture is diluted with an equal volume of water. II. Nessler's reagent: 100 gm. mercuric iodide and 70 gm. potassium iodide are dissolved in 400 c.c. water in a liter flask. 100 gm. NaOH are dissolved in 500 c.c. water, cooled, and added to the mixture with vigorous shaking. The contents of the flask are diluted to 1 liter with water, the red-brown precipitate is allowed to settle, and the supernatant solution is decanted for use. (Method of Bock and Benedict.) III. Standard: 3 c.c. standard ammonium sulphate solution (containing 1 mg. nitrogen per 10 c.c.; 0.4716 purified ammonium sulphate per liter of ammonia-free distilled water) are mixed in a 100 c.c. flask with 2 c.c. diluted acid mixture, and, after dilution to 60 c.c., with 30 c.c. Nessler's reagent and the whole made up to 100 c.c.

Method: 5 c.c. blood filtrate are placed in a large, hard-glass test tube (200 mm. x 25 mm.). One c.c. acid mixture and a quartz bead are added and the mixture is boiled vigorously until the tube is filled with dense fumes. The mouth of the tube is then covered with a watch glass and gentle boiling is continued for 2 minutes or until the solution is clear. After the mixture has cooled 70–90 seconds 15–25 c.c. water are added and, after further cooling, sufficiently more to dilute to 35 c.c., 15 c.c. Nessler's reagent are added and mixed and the color compared with the standard in a Duboscq colorimeter.

Urea (Karr's method). The urea in a sample of filtrate is changed, by the action of urease, to ammonium carbonate. This is nesslerized and compared in a colorimeter with a standard solution of urea similarly treated.

Reagents: I. Buffer solution: 14 gm. sodium pyrophosphate ($Na_4P_2O_7 . 10H_2O$) is dissolved in sufficient N/2 phosphoric acid to make 100 c.c. II. Urease solution, or paper: 15 gm. jack-bean meal with 5 gm. permutit and 100 c.c. 15% alcohol are shaken for 15 minutes in a mechanical shaker, and filtered. The filtrate may be used as the reagent or the urease may be preserved by dipping strips of ammonia-free filter paper in it and drying them. III. Nessler's reagent. IV. Standard urea solution: 0.1286 gm. urea in 200 c.c. Five c.c. of this solution (0.075 mg.N) are diluted to 100 c.c. for use in comparator.

Method: 5 c.c. filtrate are placed in a test tube with 1 drop of buffer solution and a strip (1 × 1½ in.) of urease paper. In a second tube 5 c.c. of standard solution are similarly treated and both tubes are heated in a bath at 50° for 15 minutes. The contents are then transferred to clean tubes and diluted to 22.5 cc., 2.5 cc. of Nessler's reagent are added to each and the two are compared in a colorimeter.

Creatinine (Folin-Wu method). The color produced in a portion of the blood filtrate by alkaline picrate (Jaffé's reaction) is compared with that of a standard in a colorimeter, as in Neubauer's test above.

Reagents: I. Alkaline picrate solution: 25 c.c. saturated solution purified picric acid mixed with 5 c.c. of 10% NaOH. II. Standard: 3 c.c. of a 0.1% creatinine solution in N/10

HCl plus 50 c.c. N/10 HCl, diluted with water to 500 c.c. This solution contains 0.03 mg. creatinine in 5 c.c.

Method: 10 c.c. filtrate is placed in one test tube, and 5 c.c. of II is transferred to a second tube and diluted with water to 20 c.c. Then 5 c.c. of I is added to the unknown and 10 c.c. to the standard. The two mixtures are allowed to stand for 10 minutes and then compared in the colorimeter.

Uric Acid (Benedict method). A blue color is produced by addition, to a portion of the filtrate, of arseno-phosphotungstic acid reagent and sodium cyanide. This color is compared with that similarly produced in a standard uric acid solution.

Reagents: I. 5% solution of **sodium cyanide** containing 0.2% concentrated ammonia. (Poison!). II. Uric acid reagent: One hundred grams sodium tungstate are dissolved in 600 c.c. water in a liter flask. There are then added successively 50 gms. arsenic pentoxide, 25 c.c. of 85% phosphoric acid and 20 c.c. concentrated hydrochloric acid. This mixture is boiled for 20 minutes, cooled, and diluted to 1 liter. III. Standard solution of uric acid: 9 gms. pure disodium hydrogen phosphate (Na_2HPO_4) and 1 gm. pure sodium dihydrogen phosphate (NaH_2PO_4) are dissolved in about 250 c.c. hot water and the mixture is filtered. This is then diluted to 500 c.c. with hot water and added to 200 mg. pure uric acid suspended in a few c.c. water in a liter flask. When the uric acid is completely dissolved (shake!) the mixture is allowed to cool and 1.4 c.c. (measure carefully!) of glacial acetic acid are added, and the contents of the flask are diluted to 1 liter. (Five c.c. chloroform may be added as a preservative). **A portion of this solution is diluted for use** as follows: Ten c.c. of the concentrated solution (1 mg. per 5 c.c.) are placed in a 500 c.c. flask with 250 c.c. distilled water. Twenty-five c.c. dilute (10%) HCl are added and the mixture diluted to 500 c.c. This standard contains 0.02 mg. uric acid per 5 c.c.

Method: Five c.c. filtrate are mixed in a large test tube with an equal quantity of water. Five c.c. of the diluted standard solution (0.02 mg. uric acid) are similarly treated in a second tube. Four c.c. of a 5% solution of sodium cyanide (poison!) containing 0.2% concentrated ammonia, are added to each tube followed by 1 c.c. of the arseno-

phosphotungstic acid reagent. Both tubes are then placed in boiling water for 3 minutes, cooled by immersion in cold water for 3–5 minutes, and compared in a colorimeter.

Blood sugar (Folin and Wu method). The protein-free blood filtrate is heated with alkaline copper solution, using a special tube to prevent reoxidation. The cuprous oxide formed is treated with a molybdate phosphate solution, a blue color being obtained which is compared with that of the standard.

Reagents: I. Standard sugar solution: Three standard sugar solutions should be prepared: (1) a stock solution, 1% glucose or invert sugar, made up in 0.25% benzoic acid; (2) a solution containing 0.2 mg. of sugar in 2 c.c. (5 c.c. of the stock solution diluted to 500 c.c. with 0.25% benzoic acid); (3) a solution containing 0.4 mg, of sugar in 2 c.c. (5 c.c. of the stock solution diluted to 250 c.c.). The invert sugar solution has the advantage that it can be easily prepared from pure cane sugar. II. Alkaline copper solution: Dissolve 40 gm. of pure anhydrous sodium carbonate in about 400 c.c. of water and transfer to a liter flask. Add 7.5 gm. of tartaric acid, and when the latter has dissolved add 4.5 gm. of crystallized copper sulphate. Mix and make up to a volume of 1 liter. The reagent seems to keep indefinitely. To test for the absence of cuprous copper in the solution, transfer 2 c.c. to a test tube and add 2 c.c. of the molybdate phosphate solution; the deep blue color of the copper should almost completely vanish. In order to forestall improper use of this reagent attention should be called to the fact that it contains extremely little alkali, 2 c.c. by titration (using the fading of the blue copper tartrate color as indicator), requiring only about 1.4 c.c. of normal acid. III. Phosphomolybdic acid solution: To 35 gm. molybdic acid and 5 gm. sodium tungstate, add 200 c.c. of 10% sodium hydroxide and 200 c.c. of water. Boil vigorously for 20 to 40 minutes so as to remove nearly all the ammonia present in the molybdic acid. Cool, dilute to about 350 c.c., and add 125 c.c. of concentrated (85%) phosphoric acid.

Method: Transfer 2 c.c. of the tungstic acid blood filtrate to a blood-sugar test tube and to 2 other such test tubes (graduated at 25 c.c.) add 2 c.c. of standard sugar solutions

containing respectively 0.2 and 0.4 mg. of glucose. To each tube add 2 c.c. of the alkaline copper solution II.

The surface of the mixtures must now have reached the constricted part of the tube. If the bulb of the tube is too large for the volume (4 c.c.) a little, but not more than 0.5 c.c. of a diluted (1:1) alkaline copper solution may be added. If this does not suffice to bring the contents to the narrow part, the tube should be discarded. Test tubes having so small a capacity that 4 c.c. fills them above the neck should also be discarded. Transfer the tubes to a boiling water bath and heat for 6 to 8 minutes. Add immediately (before cooling) to each test tube 2 c.c of III. When the cuprous oxide is dissolved, cool and dilute the resulting blue solutions to the 25 c.c. mark, insert a rubber stopper, and mix. It is essential that adequate attention be given to this mixing because the greater part of the blue color is formed in the bulb of the tube. Compare in a colorimeter using the standard which most nearly matches the unknown.

The two standards given, representing 0.2 and 0.4 mg. of glucose, are adequate for practically all cases. They cover the range from about 70 to nearly 400 mg. of glucose per 100 c.c. of blood.

Benedict Modification of the Folin-Wu Blood Sugar Method. A copper reagent is used which is less readily reduced by substances in the blood filtrates other than glucose, and hence is believed to give values representing more closely the true glucose concentration.

Reagents: I. Alkaline copper reagent: Dissolve 200 mg. sodium citrate and 60 gm. anhydrous sodium carbonate in about 800 c.c. of water. Dissolve 6.5 gm. pure crystallized copper sulphate separately in about 100 c.c. of water and add to the other solution while stirring. Add 9.0 gm. ammonium chloride, dilute the solution to 1 liter, and mix thoroughly. Not more than 1 month before use, add to a small reagent bottle containing about 100 c.c. of this reagent, about 2.5–3.0 gm. sodium sulphite. For occasional sugar determinations, omit addition of sulphite to the reagent but introduce 5 drops of 20% sodium sulphite into each sugar tube prior to adding the solutions. II. Tungstic acid reagent: In a liter flask dissolve 100 gm. pure sodium tungstate in

about 600 c.c. of water. Add 50 gm. pure arsenic pentoxide, 25 c.c. of 85% phosphoric acid and 20 c.c. of concentrated hydrochloric acid. Boil mixture 20 minutes. Cool, add 60 c.c. commercial formalin, 45 c.c. concentrated hydrochloric acid and 40 gm. sodium chloride. Dissolve, dilute to 1 liter and mix. This reagent contains more formalin and has a higher acidity and specific gravity than the Benedict uric acid reagent.

Method: Two c.c. of the 1:10 tungstic acid filtrate are measured into a Folin-Wu sugar tube followed by 2 c.c of the copper reagent I. Mix by side to side shaking for a moment and put tubes in boiling water for 5 minutes. The reduced copper is held in solution by the ammonium salt. Cool by immersion in cold water and add 2 c.c. of the complex tungstic acid reagent II whereupon the color development is practically immediate. After 1 to 2 minutes, dilute to the 25 c.c. mark, mix thoroughly, and compare in a colorimeter with a standard solution treated in the same way. The Folin and Wu standards may be employed.

Carbohydrate Tolerance Test: In the normal, fasting individual the ingestion of pure carbohydrate brings about a rise in blood sugar which reaches its maximum in an hour to an hour and a half and disappears within three and one half hours. In pathological conditions the maximum is often higher and the blood sugar does not fall to the normal level until after several hours.

Method: The patient, having had no food since the night before, is given 1.7 gm. of glucose per kilogram of body weight. This is best administered dissolved in water. Blood is withdrawn by venesection immediately before the administration of glucose, and at ½ hour, 1 hour, and 1½ hours, 2½ hours and 3½ hours thereafter. Sugar determinations are done on each specimen and the results plotted in the form of a curve. The total urine is collected in two 6-hour specimens following the test and examined for sugar.

The normal curve rises to 0.16% at the end of the first hour and then gradually falls, reaching normal within 3½ hours. In diabetes the entire curve is elevated and may not return to the fasting level for from 6–8 hours. In hyperthyroidism the curve is also elevated and its fall is delayed

although not to the degree characteristic of the diabetic. In Addison's disease the curve is low and flat. In diabetes, and sometimes in hyperthyroidism, the urine collected during the period of the test may contain glucose.

Blood chlorides (Whitehorn's method). The chlorides are precipitated from the blood filtrate by means of silver nitrate in the presence of nitric acid and the excess of silver titrated with standard thiocyanate solution, using ferric ammonium sulphate as an indicator.

Reagents: I. Silver nitrate solution: Dissolve 2.905 gm. of C.P. silver nitrate in distilled water, and dilute to 1 liter. Preserve in a brown bottle. 1 c.c. = 1 mg. NaCl. (It is to be noted that the silver nitrate and nitric acid are not added to the protein-free filtrate simultaneously. To do so may result in the mechanical enclosure of silver nitrate solution within the curds, and a consequent error in the positive direction.) II. Thiocyanate solution: Because the thiocyanates are hygroscopic, the standard solution should be prepared volumetrically. As an approximation about 1.7 gm. of KCNS or 1.5 gm. of NH_4CNS should be dissolved in a liter of water. By titration under the conditions specified under "Method" and by proper dilution prepare a standard such that 5 c.c. are equivalent to 5 c.c. of the silver nitrate solution. III. Ferric ammonium sulphate: The solid ferric alum is used rather than a solution, in order to insure a very high concentration in the mixture to be titrated. It is powdered in order to facilitate its solution.

Method: Because of the slight variations in the chloride content of blood, dilution in preparation of protein-free filtrates should be made very carefully and volumetric flasks may be preferred. Pipette 10 c.c of the protein-free filtrate into a porcelain dish. Add with a pipette 5 c.c. of the standard silver nitrate solution I and stir thoroughly. Add about 5 c.c. of concentrated nitric acid (sp. gr. 1.42), mix, and let stand for 5 minutes, to permit the flocking out of the silver chloride. Then add with a spatula an abundant amount of powdered ferric ammonium sulphate (about 0.3 gm.) and titrate with standard thiocyanate solution II, until the definite salmon-red (not yellow) color of the ferric thiocyanate persists in spite of stirring for at least 15 seconds.

Calculation: (5.00 (c.c. $AgNO_3$ used)) – x(c.c. KCNS used) 100 = mg. of NaCl per 100 c.c. of blood (or plasma).

Physical Characteristics of Blood Serum

	Normal	In Disease
Specific gravity.....	1.029–1.031	Lowered in nephritis with œdema, anæmia and marasmus
Refractometer value.	1.348–1.350	Follows the protein content
Freezing point δ....	–0.56° C	Abnormally low in renal insufficiency and impending uræmia

Composition of Blood Serum (per 100 c.c.)

	Normal	In Disease
Dried residue.......	18–22 gm.	Diminished in nephritis with œdema, anæmia, and marasmus
Total nitrogen......	1.04–1.2 gm.	Diminished in nephritis with œdema, anæmia, and marasmus
Protein............	6.5–7.5 gm.	Diminished in nephritis with œdema, anæmia, and marasmus
Rest-nitrogen.......	20–35 mg.	Increased in renal insufficieney and impending træmia
Urea..............	30–40 mg.	Increased in renal insufficiency and impending uræmia
Uric acid..........	2.0–3.5 mg.	Increased in gout and renal insuffieiency
Creatinin..........	1.0–1.5 mg.	Increased in renal insufficiency
Sugar.............	70–110 mg.	Increased in diabetes mellitus
Chlorides..........	560–600 mg.	Increased in nephritis with œdema
Calcium...........	9–11 mg.	Diminished in tetany and in severe nephritis

MORPHOLOGICAL CHARACTERISTICS OF THE BLOOD

The red blood corpuscles (**erythrocytes**) are normally between 6.7 and 9.3μ in diameter (1μ = 1/1000 millimeter) average 7.8μ. Large red blood corpuscles (megalocytes, 10

to 15μ) are derived from megaloblasts and are found chiefly in anæmia and particularly in pernicious anæmia. The red blood corpuscles in pernicious anæmia and particularly the megalocytes are rich in hæmoglobin, and as a result stain deeply with eosin. In sharp contrast are the abnormally pale, hæmoglobin-poor cells in chlorosis and the secondary anæmias. Dwarf red blood cells (6 to 2.2μ but of normal form) are also found often in anæmia.

Red blood corpuscles of irregular shape are called **poikilocytes** (pear- club- biscuit-shape) and are found in all forms of anæmia. One may confuse with poikilocytes red blood corpuscles viewed in their long axis or cells which may have been injured in the preparation of the specimen. True poikilocytes are to be made out in the fresh, unstained blood preparation. **Microcytes** are small, round corpuscles, rich in hæmoglobin, which occur from time to time in severe anæmia and may possibly be produced by the shrinking of normal red blood corpuscles. In certain forms of anæmia peculiar long processes, which seem to show amœboid movement, are visible arising from the red blood corpuscles. This alteration is without pathological significance.

Nucleated red blood corpuscles (**erythroblasts**) may be present in all forms of anæmia and are particularly numerous during the active stages of blood regeneration. They represent young, immature forms of the normal, unnucleated, red blood corpuscles. Two types of nucleated red blood corpuscles are to be differentiated: 1. Normoblasts, the size of the normal red blood corpuscles, which are immature forms of the normal red blood corpuscles, and show darkly staining nuclei, and 2. Megaloblasts, larger cells with large, faintly-staining, honey-combed nucleus not so sharply marked off from the cytoplasm. These are immature forms of megalocytes and represent the type of development of red blood corpuscles which normally takes place during early embryonic life. The hæmoglobin-containing protoplasm of the nucleated red blood cell may stain violet rather than pure red (acidophile) with the usual staining methods since it also takes up the basic dyes.

The generation of red blood corpuscles takes place norm-

ally in the red bone marrow. If, as a result of anæmia, e.g. after a large hæmorrhage, active regeneration of red blood corpuscles becomes necessary the number of nucleated red blood corpuscles in the bone marrow is conspicuously increased. These are transformed into normal red blood corpuscles with disappearance of their nuclei. The fatty bone marrow of the long bones, e.g. the femur, may, in severe anæmia, be re-converted into blood-forming tissue as in children. In long-standing severe anæmias, e.g. pernicious anæmia, blood-forming (myeloid) tissue may also appear in the spleen, liver and lymph glands, a reversion to early embryonic life. If regeneration in the bone marrow and in other organs fails to take place the resulting anæmia is spoken of as "aplastic." In such cases the white blood corpuscles of the myeloid series, i.e. the poly-

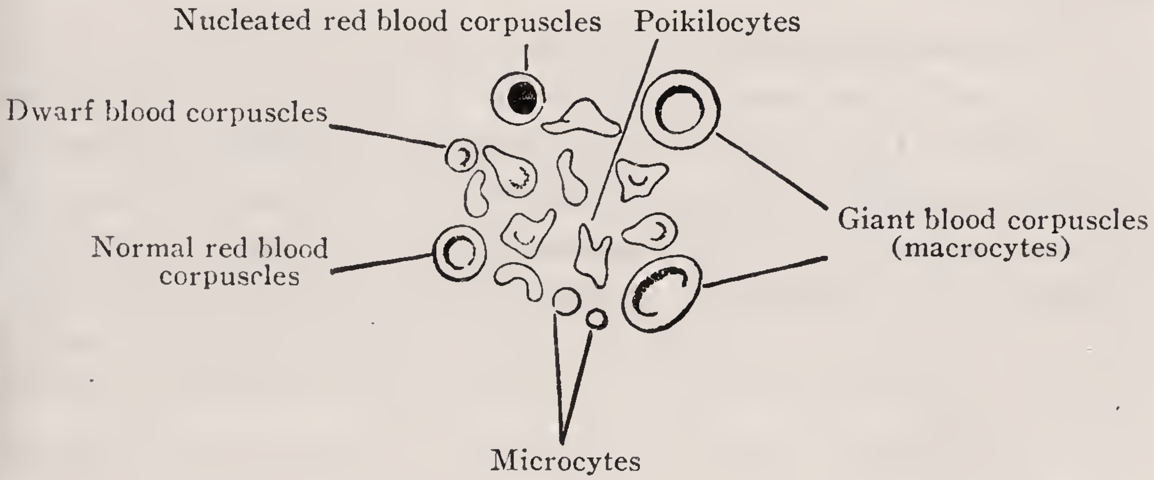


FIG. 52.

morphonuclear leucocytes and their precursors, are greatly decreased in number in the blood stream, and nucleated red blood corpuscles are altogether absent.

Nucleated red blood corpuscles are to be made out only with difficulty in the unstained preparation on account of the yellowish-green color of their protoplasm. Their unequivocal demonstration involves the staining of the dried preparation.

The red blood corpuscles in the dried preparation take up the "acid" dyes, e.g. eosin. Under pathological conditions, e.g. severe anæmia, some of the corpuscles take up both acid and basic dyes, assuming a mixed color composed of both, e.g. violet (polychromatophilia). Concerning the absorption of acid and basic dyes see chapter on Microörganisms.

Newly-formed red blood corpuscles may be distinguished

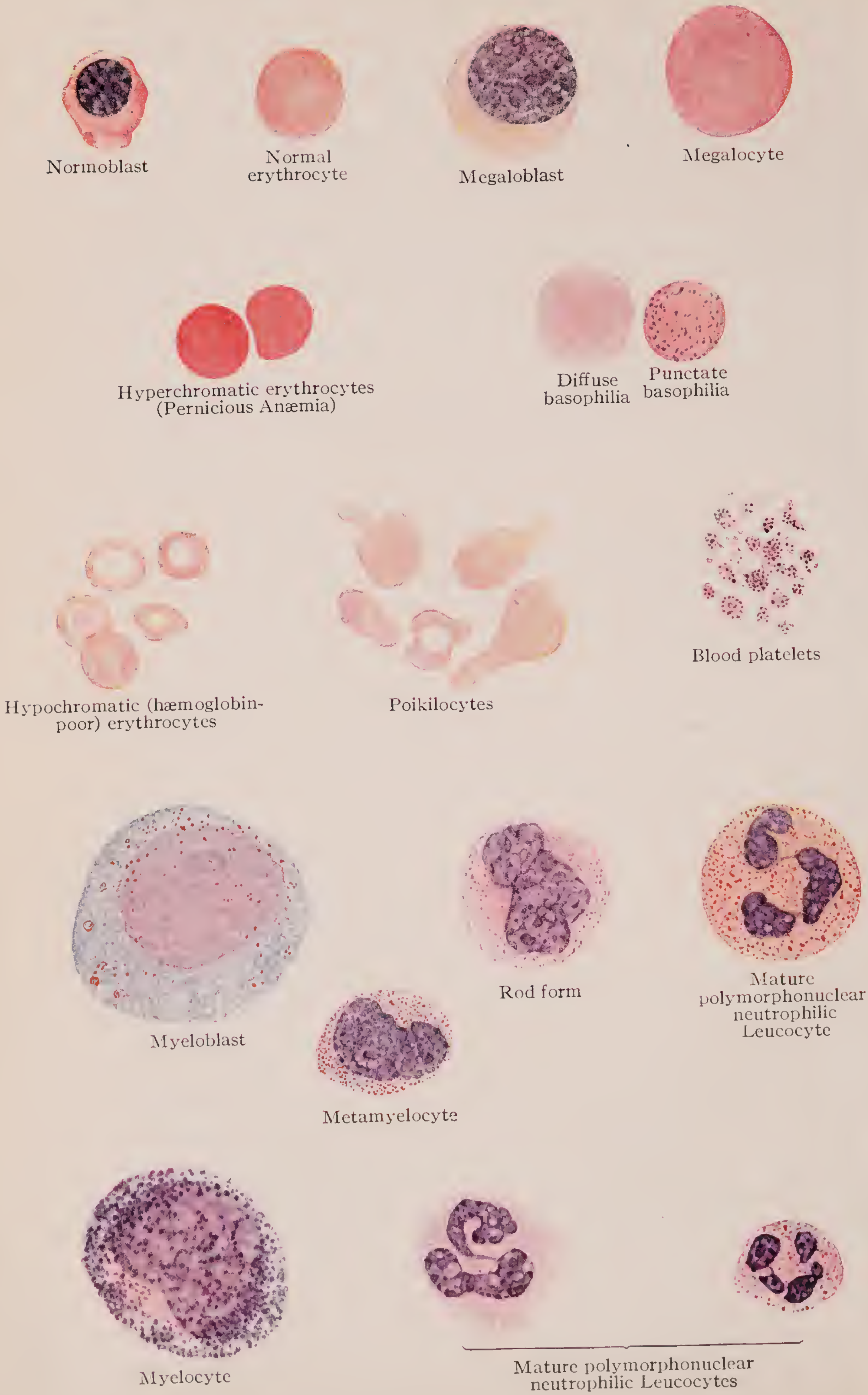
in the circulating blood by the fact that they contain within their cytoplasm a delicate reticulum which stains with cresyl blue. Such reticulocytes represent an intermediary stage between the immature, nucleated red cells and the older erythrocytes which stain uniformly. Reticulated red cells are present in normal blood (0.5–1.0%). The ability of the bone marrow to generate new cells and, as well, the rate of this production may be judged from the degree of reticulocytosis. Such cells are not seen in the blood of aplastic anæmia; they are present in large numbers in the blood of pernicious anæmia at the beginning of a remission. In patients with pernicious anæmia who receive adequate amounts of liver or liver-extract the remission thus induced is heralded by an increase in reticulocytes to 10–20% or more. (See page 164 for staining method.)

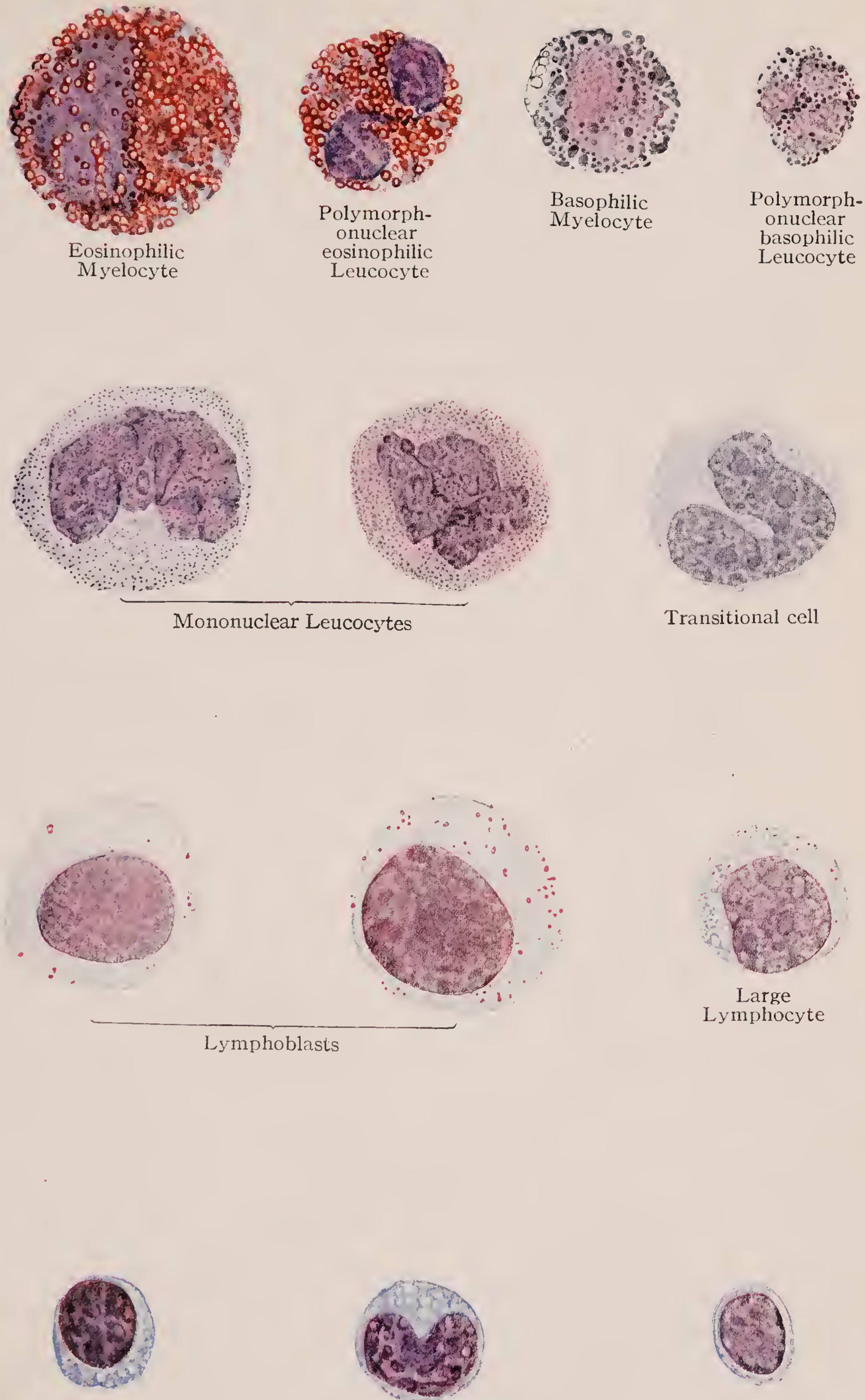
The **blood platelets** (Bizzozero) are colorless, flat, round plates 2–4μ in diameter. Outside the vessels they disintegrate very rapidly. They appear in constantly changing numbers in the blood and play an important rôle in thrombus formation (platelet thrombi), and in the coagulation of fibrin. The blood platelets arise presumably as products of the segmentation of large cells in the bone marrow, the megakaryocytes, which may also appear from time to time in the circulating blood. The blood platelet count is normally 250,000—300,000 per cu. mm. blood. In thrombopænic purpura they are reduced in number, a finding which corresponds with the increased bleeding and clotting time; in chlorosis and secondary anæmia they are abnormally numerous.

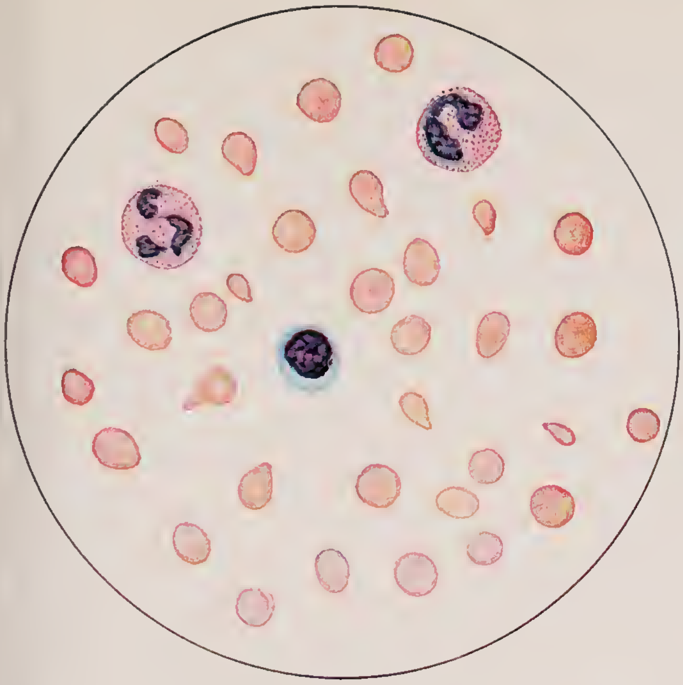
Among the **white blood corpuscles** the following forms are to be differentiated (see plate):

Lymphocytes about the size of a red blood corpuscle containing a round, compact nucleus with a distinct nucleolus. The cytoplasm of the lymphocyte forms only a narrow layer about the nucleus and stains deeply with basic anilin dyes, e.g. with methylene blue. With Giemsa's stain many lymphocytes show reddish granules (azure granules).

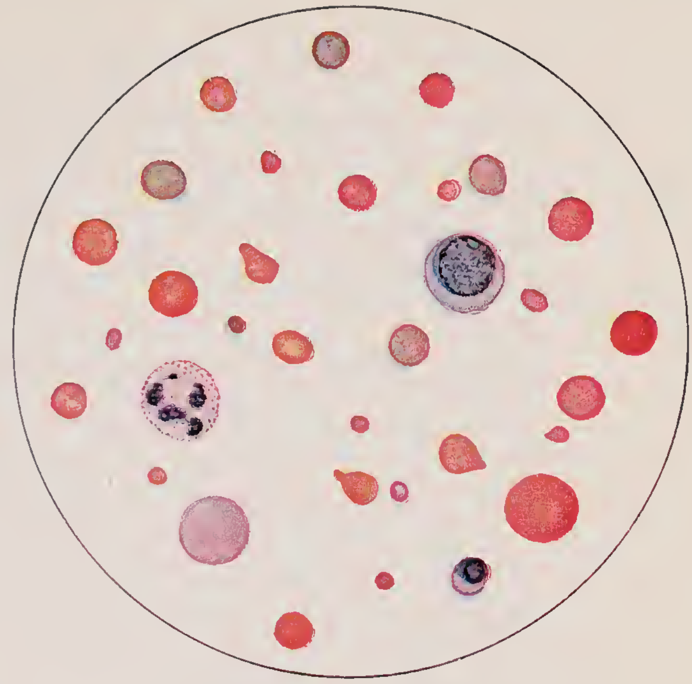
In addition to these **small** lymphocytes Ehrlich distinguished **large** lymphocytes having a large nucleus, poor in chromatin, and a somewhat wider layer of cytoplasm, but


Normoblast
Normal erythrocyte
Megaloblast
Megalocyte
Hyperchromatic erythrocytes (Pernicious Anæmia)
Diffuse basophilia
Punctate basophilia
Hypochromatic (hæmoglobin-poor) erythrocytes
Poikilocytes
Blood platelets
Myeloblast
Metamyelocyte
Rod form
Mature polymorphonuclear neutrophilic Leucocyte
Myelocyte
Mature polymorphonuclear neutrophilic Leucocytes

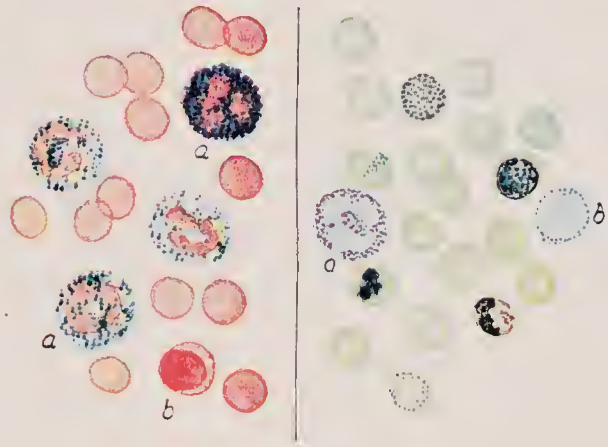

Eosinophilic Myelocyte
Polymorphonuclear eosinophilic Leucocyte
Basophilic Myelocyte
Polymorphonuclear basophilic Leucocyte
Mononuclear Leucocytes
Transitional cell
Lymphoblasts
Large Lymphocyte
Plasma cell
Rieder cell
Small Lymphocyte



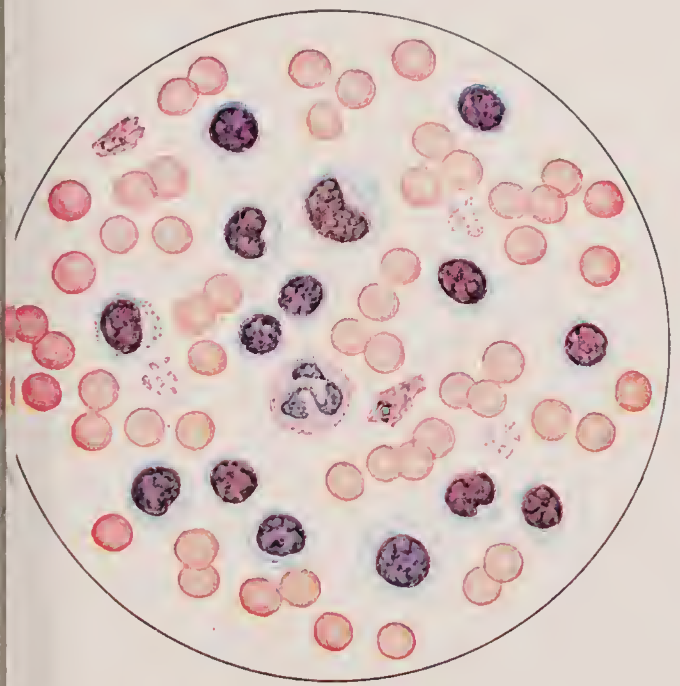
Hypochromic anaemia



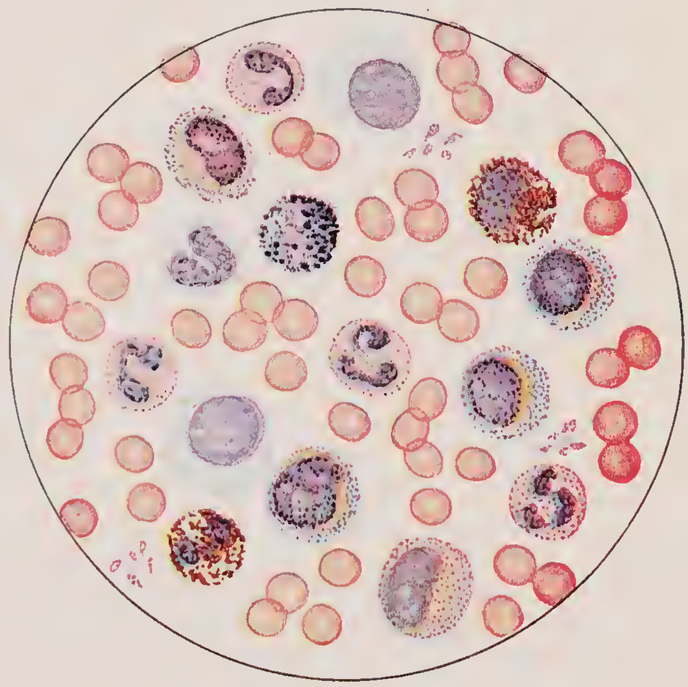
Hyperchromic anaemia



Oxidase reaction Supravital stain
(a = polymorphonuclear leucocytes, b = lymphocytes)



Lymphatic leukaemia



Myeloid leukaemia

otherwise similar to the smaller forms (round nucleus, basophilic, agranular protoplasm). Large lymphocytes are encountered only in small numbers in the normal blood. They appear chiefly under pathological conditions, particularly with the various types of benign and malignant hyperplasia of the lymph glands. Above all they are seen in large numbers in acute lymphatic leukæmia. Very large lymphocytes with an almost undifferentiated, incompact, nucleus are known as lymphoblasts, i.e. still more immature forms. These appear in the more severe cases of lymphatic leukæmia.

The lymphocytes constitute approximately 25% of all the white blood corpuscles in the blood of the adult (in children 50%). In lymphatic leukæmia they are conspicuously increased (80–95%). An increase in the number of lymphocytes to 40–60% of the total white corpuscles takes place in Basedow's disease and other forms of hyperthyroidism, as well as in status lymphaticus. The lymphocytes are formed in the lymphatic tissue which is distributed over the entire body, and particularly in the lymph glands, the follicles of the spleen, the tonsils, the intestines and other organs; they are also present in the bone marrow. In lymphatic leukæmia their number is enormously increased in the large lymph glands as well as in the spleen and bone marrow. A decrease in the number of lymphocytes (lymphopænia) occurs (down to 10–5%) in all those diseases in which the lymph glands or tissues are extensively overgrown and suppressed by granulation tissue, carcinoma or sarcoma, e.g. in granuloma and generalized glandular carcinomatosis.

Large mononuclear leucocytes are large cells with a thick faintly-staining layer of finely granular cytoplasm. These cells are normally present in the blood but only in small numbers. Similar cells containing a lobulated nucleus were designated as "transitional," by Ehrlich since he believed that they represented a stage of transition of the polymorphonuclear neutrophilic leucocytes, a supposition which has since been shown to be incorrect. Large mononuclear cells and the so-called "transitionals" compose together from 1–10% of the total white corpuscles of the normal blood. To this group is now applied the term **monocytes.**

Polymorphonuclear leucocytes are characterized by a lobulated nucleus rich in chromatin, which stains deeply with basic dyes and contains no nucleolus. These cells are larger than the lymphocytes, their cytoplasm is acidophilic, i.e. stains faintly pink, and contains a large number of fine granules which stain pink or red-violet with the stain of Jenner-May, or carmine with that of Giemsa (neutrophilic granules). In the normal blood the polymorphonuclear leucocytes constitute by far the greater proportion of the white blood cells, about 70%. The polymorphonuclear leucocytes are distinguished from other white blood corpuscles by their motility; they wander out from the blood vessels into inflamed tissue. The pus in acute inflammation contains almost exclusively this form of leucocytes, which are, for this reason, designated as pus corpuscles. Since the polymorphonuclear leucocytes may also wander to the surface of mucous membranes, they are to be found in secretions of the air passages, of the mouth, pharynx, gastro-intestinal tract and bladder. Dependent upon the maturity of the cell the nucleus is more or less lobulated, i.e. leucocytes with unlobulated nuclei are younger, those with many nuclear lobules are the older forms. (Arneth.)

The form of the nucleus of the neutrophilic leucocyte, and in particular the number of the nuclear segments, is of practical diagnostic significance. Three types are distinguished: (1) segmented nuclei whose lobules are connected only by filaments, (2) bent into a knot or an S, and (3) young forms shaped like a sausage. The last two types make up not more than 6% of the normal neutrophile count. With any infection their proportion is increased.

The polymorphonuclear **neutrophilic leucocytes** contain enzymes and in particular a proteolytic ferment, which is freed upon the disintegration of the cell and exerts its autolytic action in pus, and in the resolution of pneumonia. In addition they contain an oxidase and, inasmuch as this ferment is unique to the polymorphonuclear neutrophilic leucocytes and their precursors, and is not found in some monocytes, e.g. lymphocytes, the so-called oxidase reaction (see

page 165) may be used to differentiate the early forms of the myeloid and lymphatic series.

Eosinophilic leucocytes (so called by Ehrlich) contain in their protoplasm large fatty, refractile granules which stain deeply red with eosin. Since eosin is an acid dye these granules may be classified as acidophilic in contrast to those which are basophilic or neutrophilic. Eosinophilic leucocytes are present in the normal blood in small numbers, about 1–4% of all the white corpuscles. In myeloid leukæmia the absolute number of eosinophilic cells is considerably increased. In the normal blood the eosinophilic cells usually have a two-lobed nucleus. In leukæmic blood large eosinophilic cells appear which have a large, pale, round nucleus of the type of the myelocyte. The eosinophilic leucocytes are increased (to 10% and more) in the blood in cases of bronchial asthma and trichinosis (to 60%). Also in many cases of helminthiases, tape-worm, echinococcus, ankylostoma, ascaris, trichocephalus, an increase in the eosinophilic leucocytes is demonstrable. Finally, there is sometimes "eosinophilia" with scarlatina, with diphtheritic enteritis and (up to 50%) in many severe skin diseases, and in periarteritis nodosa as well as now and then with malignant neoplasms, e.g. sarcoma, granuloma, and carcinoma.

Basophilic leucocytes: Certain polymorphonuclear leucocytes which contain in their protoplasm large granules were named by Ehrlich "Mast cells." Their granules are basophilic, i.e. stain deeply with the basic analin dyes, but assume a different color from that of the nucleus; upon staining with methylene blue they appear not blue but violet (metachromatic), while the nucleus colors faintly blue. The granules of Mast cells are very easily soluble in water, and, therefore, in preparations which have been repeatedly washed, may appear as vacuoles. Mast cells are present in normal blood only in small numbers, but are increased in myeloid leukæmia. Leucocytes are now and then encountered which contain, in their cytoplasm, a variety of granules, i.e. both eosinophilic and basophilic.

Myelocytes represent a type of leucocyte which is not normally present in the blood. They derive their name from

the fact that they are present in great numbers in the normal red bone marrow. They vary in size, are often very large, and contain a large, round, honey-combed, faintly-staining nucleus with a nucleolus. It is safe to assume that the younger nucleus shows a less compact structure and stains faintly, while the mature and older nucleus is more compact and stains more deeply (is richer in chromatin). In the cytoplasm of myelocytes are fine neutrophilic granules similar to those found in polymorphonuclear leucocytes. Since, in the nuclei of these myelocytes, in the bone marrow, as well as in the circulating leukæmic blood, mitotic figures are sometimes to be observed, and since, between the myelocytes and the polymorphonuclear leucocytes, several transitional forms are found, one may assume that myelocytes represent early, immature forms of the polymorphonuclear leucocytes, which under normal conditions would not appear in the blood. Myelocytes differ from the large mononuclear cells described above in that the latter contain no granules and show, with Giemsa's stain, a grayish-blue cytoplasm, while that of the myelocytes stains blue or faintly pink. Myelocytes are found in enormous numbers in the circulating blood in myeloid leukæmia, and in smaller numbers in severe infectious diseases (sepsis), and in many affections of the bone marrow.

Myeloblasts are cells of the type of myelocytes but differ from these in that their cytoplasm stains blue and contains no granules. Since all forms intermediate between non-granular myeloblasts and granular myelocytes are encountered, it is assumed that the former are precursors of the myelocytes. They are present with any condition which brings about stimulation of the bone marrow and are particularly numerous in severe myeloid leukæmia. Morphologically they are scarcely distinguishable from the large lymphocytes and may only be identified with certainty when myelocytes and intermediate granular forms are also present. In contrast with lymphocytes and lymphoblasts, the myeloblasts give the typical oxidase reaction. The intermediate forms between myeloblasts and myelocytes are spoken of as promyelocytes

and those between myelocytes and mature polymorphonuclear leucocytes are called metamyelocytes.

Turk "irritation forms" are cells with large basophilic, usually grossly vacuolated, cytoplasm and a relatively small, lobulated, compact nucleus. It is probable that they are pathological myeloblasts. They appear in various infectious diseases (scarlatina), anæmia and leukæmia.

The **red blood cell count** in normal men is on the average 5,300,000 per cu. mm.; in women, 4,800,000 per cu. mm. The white blood count varies normally between 5,500 and 8,000 per cu. mm.

A decrease in the erythrocyte count (oligocythæmia) is present in most forms of anæmia. Increase in the erythrocyte count is designated as **polycythæmia rubra;** and may amount to 6, 8, or even 14 million per cu. mm. The red cell count rises in normal individuals if they remain at high altitudes and falls to normal soon after return to sea level. With the inspissation occurring in cholera, and with the chronic venous stasis in many forms of heart disease, the red blood count is increased. A severe grade of polycythæmia occurs also as an independent disease, associated with splenomegaly. In many cases polycythæmia is associated with high blood pressure (polycythæmia hypertonica). Such patients show suffusion of the face, tend to suffer from headache and vertigo and are particularly prone to apoplexy.

The **leucocyte count** may also be strikingly decreased (below 5,500) or increased (above 8,000 per cu. mm.). The former condition is designated as leucopænia, the latter as leucocytosis. The various forms of white blood corpuscles may take part in varying degrees in any increase or decrease in the leucocyte count. Thus leucopænia, with particular decrease in the polymorphonuclear cells and disappearance in the eosinophiles, occurs in typhoid, measles and sometimes in severe sepsis. A sudden fall in the lymphocyte count is a sign of serious import in these infectious diseases. Leucocytosis, with conspicuous increase in the number of polymorphonuclear leucocytes, is a constant finding in all those infectious processes which involve an acute and localized

inflammation about which leucocytic infiltration is so characteristically seen, e.g. erysipelas, scarlatina, diphtheria, purulent meningitis and typhus, and particularly pneumonia. Here the leucocytosis in the days immediately before the crisis may reach a high level (often 20,000) and is to be regarded as a favorable sign. In purulent, inflammatory conditions in the abdomen leucocytosis also tends to appear, and the white blood count may be of diagnostic value in suspected cases of appendicitis or gall-bladder disease. In the case of an overwhelming infection with an organism of high virulence (e.g. intestinal perforation with peritonitis) instead of a leucocytosis there may result a leucopænia, a distinctly unfavorable sign. In addition to the infectious diseases leucocytosis may also be present with sarcoma and carcinoma, as well as with other diseases, which, in their late stages, are characterized by anæmia and cachexia (cachectic leucocytosis).

Examination of the blood

It is sometimes sufficient simply to take up a drop of blood obtained by pricking the ball of the finger or lobe of the ear, upon a clean cover slip, to place the cover slip upon a clean slide and to examine with the high power of the microscope. The red corpuscles are seen lying in rouleaux and there may be visible one or two leucocytes per field. The presence of a large number of leucocytes per field (10, 20 or more) indicates leucocytosis; the degree of leucocytosis may only be determined by the use of a counting chamber. The blood platelets may be brought into view by pricking the finger through a drop of 14% magnesium sulphate solution. In place of this solution one may use a dilute solution of methylene blue in 0.6% sodium chloride solution which stains the platelets, the nuclei of the leucocytes and of the nucleated red blood corpuscles.

More exact information is to be obtained by **staining the dried smear.** A small drop of blood obtained from the finger tip is taken up on a slide and spread over it by drawing the end of a second slide across the first. Both slides must be cleaned with the utmost care (washed and rinsed in concentrated sulphuric acid, distilled water, alcohol and ether,

dried and polished with clean linen). This preparation is allowed to stand in the air until completely dry and is then fixed by placing for 5–10 minutes in absolute methyl alcohol. In the usual staining technique methyl alcohol is already present in the stain and preliminary fixation is therefore not required. (Smears may be more easily prepared by the cover-slip method. A small drop of blood is taken up on a clean cover slip and a second cover slip is placed over it. The blood spreads out between the two glass surfaces; just as its spread begins to slow, the cover slips are quickly drawn apart horizontally. Ed.)

Staining methods

Jenner-May: Eosin is used as an acid stain, methylene blue as a basic. This method has the advantage that preliminary fixation of the preparation is not required. The stain may be obtained in the form of powder which is later dissolved in absolute methyl alcohol in a concentration of 0.25–0.50%, filtered and placed in a closed vessel. The thoroughly dried smear is placed in this mixture for 2 minutes and then rinsed with **distilled water.** The preparation is then dried with blotting paper, mounted in cedar oil and examined with the oil immersion lens. With this stain the red blood corpuscles are colored red, the nuclei blue, the eosinophilic granules deep red; the neutrophilic granules appear as small pink dots, and the mast cell granules a deep violet.

Giemsa's modification of Romanowski's stain: In this stain methylene azure is formed by the oxidation of methylene blue; this azure forms a compound with eosin. **Method:** The dried preparation is fixed in absolute methyl alcohol for 2–3 minutes, dried between blotting paper and stained for 10–15 minutes. The stain should be prepared freshly before using. Wash with water, dry and mount in balsam. The red corpuscles appear red, the nuclei of the leucocytes and of the nucleated red blood corpuscles reddish-violet, the eosinophilic granules light red, the neutrophilic granules pale violet, and the basophilic protoplasm of the lymphocytes blue.

If the preparation be first stained with the Jenner-May

method and then fixed and stained by the Giemsa method (combined stain of Pappenheim), strikingly clear results may be obtained. The accompanying plate is drawn from preparations stained by this combined method.

Wilson's stain: Dissolve 1 gm. of methylene blue in 100 c.c. of distilled water. Next dissolve 2.0 gm. of silver nitrate in 50 c.c. of distilled water. To the silver solution add a 5% caustic soda solution until the silver oxide is completely precipitated. Wash the precipitated silver oxide several times with distilled water. Solution I. To the moist silver oxide add 2 gm. of methylene blue dissolved in 200 c.c. of a 0.5% solution of sodium bicarbonate in distilled water. Gently boil this silver oxide methylene blue mixture in a rather deep porcelain dish for 30 minutes, stirring occasionally. Pour off (and preserve) about 1/3 of the contents of the dish into a 200 c.c. graduated cylinder. Add to the contents of the dish an amount of boiling distilled water, equal to that poured into the cylinder, and boil again for 30 minutes. Again pour off and preserve 1/3 of the contents of the porcelain dish. Then boil the remaining contents of the dish for another 30 minutes, not adding additional water. Now add the contents of the dish to the portions previously preserved and set aside and make up the total volume with water to 200 c.c. Filter through a coarse filter into a 500 c.c. beaker and immediately add to it:

Solution II. For this solution dissolve 1 gm. of yellow, water-soluble eosin in 200 c.c. distilled water. Allow this mixture of the two solutions to stand about 30 minutes and then filter, collecting the precipitate on a hard filter paper. The precipitate may be dried in an incubator or hot air oven at 60° C. The yield of dry precipitate is about 1.7 gm. For the staining fluid dissolve 0.2 gm. in 50 c.c. pure methyl alcohol.

Method: Six to 8 drops of stain are placed on the smear, held horizontally with forceps, and allowed to remain 60 seconds. An equal quantity of water is then added and the mixture is left in contact with the smear for 4 minutes, after which it is washed off with a stream of distilled water.

Reticulocyte stain: Reagents: I. A 1% solution of cresyl blue in 0.85% salt solution. II. A 1% solution of potassium

oxalate in 0.85% salt solution. Before use 1 part of I is mixed with 5 parts of II.

Method: Smears of the stain are pulled on cover slips (see above) and allowed to dry. The excess of stain is removed by polishing with clean linen. Upon these treated cover slips blood smears are pulled and, after drying, counterstained by Wilson's method.

Oxidase reaction: (Goodpasture's method.) Formula: Sodium nitroprusside 0.05 gm., benzidine (C.P.) 0.05 gm., basic fuchsin 0.10 gm., alcohol (95%) 100 c.c. Dissolve nitroprusside in as little water as possible (2 c.c.), mix with the alcohol, and then dissolve the other reagents. Before using add 1 drop fresh hydrogen peroxide to 10 c.c. stain.

Method: Cover the fresh blood smear with stain (6–8 drops) and fix for 1 minute. Add an equal quantity of distilled water and stain 5 minutes. Wash with water, dry, and mount in balsam. The granules of the polymorphonuclears, eosinophiles, myelocytes and myeloblasts stain deeply blue. Lymphocytes stain pale red and erythrocytes buff.

Counting blood corpuscles

The blood cell count is best obtained in the apparatus of Thoma-Zeiss or some modification thereof. This apparatus consists of a small capillary pipette into which the blood is drawn, and in which it is diluted, and a counting chamber. Blood is drawn into the pipette up to the mark 1.0 from a drop obtained by pricking the ball of the finger; the **diluting fluid** is then drawn into the pipette until the contents reach the mark 101. (As a diluting fluid Hayem's solution is usually employed: Bichloride of mercury 0.5, sodium sulphate 5.0, sodium chlorate 1.0, distilled water 200 c.c.) The pipette and its contents are well shaken, the capillary portion is emptied of the first few drops and a small drop is then placed in the middle of the counting chamber; the well-cleaned cover slip of the apparatus is then placed upon the preparation and the corpuscles enumerated in a certain number of the squares drawn upon the base of the chamber. From this number, knowing the capacity of the chamber, one may calculate the cell count per cubic millimeter of blood. The Thoma-Zeiss counting chamber has a depth of 0.1 mm.; the smaller squares

are 1/400 sq. mm. in area; hence the space over a single such square represents 1/4000 cu. mm. or that over every 4 such squares 1/1000 cu. mm. The red blood count is therefore to be obtained by multiplying the average number of cells in each small square (the sum of the cells counted divided by the number of squares covered) by 400,000. Or the squares may be covered in series of four, the average calculated and the result multiplied by 100,000. With high erythrocyte counts and in polycythæmia it is advisable to use a blood dilution of 1:200 instead of 1:100 (up to the mark 0.5 on the pipette).

The white blood cells are counted using a similar pipette which makes possible a dilution of the blood 1:10. As a diluting fluid 1% acetic acid in water may be used; by this solution the red blood corpuscles are destroyed while the leucocytes remain visible. The leucocytes over the entire area of the ruled portion of the chamber are counted. This represents an area of 1 sq. mm. and since the chamber has a depth of 1/10 mm. the result represents the number of leucocytes in 1/10 cu. mm. Since the blood was diluted 1:10 the leucocyte count per cu. mm. of blood is obtained by multiplying the above result by 100.

Various modifications of this counting chamber ruling have been developed. The most useful is that of Neubauer (incorporated in the new Levy-Hauser apparatus). The ruling is divided into 400 small squares of 1/400 sq. mm. each. These squares are divided into 25 groups of 16 each by a double line which appears under the microscope as a transparent boundary.

Differential white blood cell count. The relative numbers of the various white blood corpuscles in the blood may be determined by the following method: The total white blood cell count is first made in the counting chamber. In a stained preparation made at the same time 3–500 white corpuscles are counted and identified. From the data so obtained it is possible to calculate the percentage or absolute frequency of the various forms of leucocytes. In the table on page 170 are given the differential white blood cell counts obtained in various blood diseases.

Platelet count: For this purpose a number of methods have been devised none of which is absolutely accurate. A simple method is that of Fonio: A red blood cell count is first made. In a stained smear prepared at the same time one enumerates the number of platelets seen while counting a thousand red cells. The number of platelets may thus be calculated; there is usually, in the normal, one platelet to every 15 red blood cells. (**The method of Wright and Kinnicutt:** Blood is drawn up to 1 in the diluting pipette and diluted 1:100 with a solution containing 2 parts of 3/10% brilliant cresyl blue and 3 parts of 1:1500 potassium cyanide. By this mixture the red blood cells are made invisible and the platelets stained a faint blue. Counting is carried out in a counting chamber. Ed.)

In the normal individual there are present 250,000 to 300,000 platelets per cu. mm. A striking decrease in the platelet count takes place in certain types of purpura, while in polycythæmia an increase is often encountered.

The **hæmoglobin content** may be estimated by the use of the hæmoglobinometer of Sahli.

In the Sahli apparatus a standard hæmatin solution is contained in a sealed narrow glass tube. By means of a fine pipette 20 cu. mm. of blood are drawn up from a drop on the finger tip and immediately transferred to a small, calibrated tube. Into this tube there has previously been placed a small quantity (up to the mark 10) of 1/10 normal hydrochloric acid. The mixture is allowed to stand for a few minutes, until the red hæmoglobin of the blood has been changed by the hydrochloric acid into brown acid hæmatin. Water is then added drop by drop until the color in the open tube is exactly that of the sealed standard tube. With normal blood the two tubes become equal in color at a dilution of about 100 while in hæmoglobin-poor specimens this point is reached at a lower dilution. The percentage of hæmoglobin may be read directly from the scale on the side of the tube. In blood with a very low hæmoglobin content it is sometimes advisable to use 20 cu. mm. of blood and to divide the result by 2. The standard tube of the Sahli apparatus fades upon prolonged exposure to light and should, therefore, be calibrated

frequently. Recently there have been prepared glass rods of a color corresponding to the standard solution.

An improvement of the Sahli principle is incorporated in the colorimeter of Autenrieth-Kœnigsberger. The standard is contained in a glass wedge which may be moved in its long axis. Only a small portion of the wedge is visible through a narrow window. The blood to be examined is placed in the glass trough of the apparatus and mixed with 1/10 normal hydrochloric acid. Color comparison is carried out by raising or lowering the wedge and the hæmoglobin content read off on the scale.

Color Index. The relative proportion of hæmoglobin to red blood cells is to be calculated by the following formula:

$$\frac{\%\ \text{hæmoglobin}}{\text{RBC (in hundred thousands)} \times 2} = \text{color index.}$$

Thus in a specimen containing 50% hæmoglobin and 2,500,000 red cells the color index $= \frac{50}{25 \times 2} = 1.$

According to this formula the normal color index is 1; if the hæmoglobin content be diminished out of proportion to the red cell count the color index is less than 1, whereas if it be disproportionately increased it is greater than 1; i.e. each red corpuscle contains a larger amount of hæmoglobin than in the normal blood. The color index tends to be reduced in chlorosis and secondary anæmia and to be greater than 1 in pernicious anæmia and sometimes in myeloid leukæmia.

DIAGNOSIS OF BLOOD DISEASES

During the twenty-four hours following a sudden and severe loss of blood, e.g. after a gastric hæmorrhage, both red count and the hæmoglobin content fall strikingly (to 50% normal and under). This is brought about chiefly by the passage of water from the tissues into the blood, whereby the normal blood volume is maintained at the cost of dilution. The white blood count, on the other hand, does not fall but tends rather to rise (posthæmorrhagic leucocytosis). In the period of regeneration which follows, the red blood count tends to rise more rapidly than the hæmoglobin content, so that, for a

certain time after the red blood corpuscles have reached the normal number, the hæmoglobin is still considerably below normal. The color index is, therefore, less than 1.

In other forms of **secondary anæmia**: in cancer, tuberculosis, Banti's disease, malaria, lead poisoning, ankylostomiasis, nephritis, etc. the red blood count is also proportionately higher than the hæmoglobin content and the color index is correspondingly reduced. Here, too, the number of white blood corpuscles may be increased, particularly the polymorphonuclear forms.

In **chlorosis** the hæmoglobin is conspicuously reduced, though the red blood count may be only slightly below normal. The red cells, therefore, appear very pale, particularly in their centers, and the color index is low. In this condition the white blood count tends to be normal or only slightly increased. The number of blood platelets is usually high and clotting is accelerated. The blood picture in chlorosis is, thus, almost identical with that in the stage of regeneration in post-hæmorrhagic anæmia. It is, therefore, almost impossible to differentiate chlorosis by blood examination alone from the secondary anæmia resulting from a severe hæmorrhage, e.g. with gastric ulcer or abortion.

In progressive **pernicious anæmia** the red blood count may be very low, often 1,000,000 or even 500,000. The hæmoglobin is, however, not reduced in the same proportion, so that the red blood cells appear richer in hæmoglobin than normal and stain more deeply with eosin. The color index is above the normal (greater than 1), a finding which is almost pathognomonic of pernicious anæmia. In addition the red corpuscles vary in size and form (poikilocytosis). Also characteristic of pernicious anæmia is the appearance of very large red blood corpuscles (megalocytes) and particularly large **nucleated** forms (megaloblasts). The white blood count is reduced (in contrast to secondary anæmia). The platelet count and the coagulability of the blood are sometimes below normal. In contrast with that in chlorosis the blood serum in pernicious anæmia is strikingly dark in color.

The blood picture in **bothriocephalus anæmia** is so similar to progressive pernicious anæmia that a differential diagnosis is often extremely difficult.

Typical Blood Counts of Various Blood Diseases

	Normal (Average)	Idiopathic Hypochromic Anæmia and Chlorosis	Pernicious Anæmia	Leucocytosis[1]	Chronic Myeloid Leukæmia	Chronic Lymphoid Leukæmia
R. B. C.	Male 5,300,000 Female 4,800,000	4,350,000 = 87%	1,200,000 = 24%	4,655,000 = 93%	2,750,000 = 55%	2,500,000 = 50%
Hb.	Male 16 gm. Female 14 gm.	56%, (8.1 gm.)	37%, (5.4 gm.)	90%, (13.0 gm.)	50%, (7.3 gm.)	45%, (6.5 gm.)
Color Index	1	56/87 = 0.64	37/24 = 1.54	90/93 = 0.97	50/55 = 0.99	45/50 = 0.9
W. B. C.	7,000 per cu. mm.	5,700	2,500	19,600	460,000	500,000
Lymphocytes	27% = 1,890	44% = 2,508	45.2% = 1,130	10% = 1,960	1% = 4,600	99% = 495,000
P. M. N.	66% = 4,620	53% = 2,921	53.5% = 1,337	84.5% = 16,562	40% = 184,000	1% = 5,000
Myelocytes	0	0	0	0	42.9% = 197,340	0
LM. & T. (Monocytes)	4% = 280	0.5% = 28.5	1.3% = 32.5	5.5% = 1,078	0.1% = 460	0
P. M. E.	2.5% = 175	2% = 114	0	0	6% = 27,600	0
Mast Cells	0.5% = 35	0.5% = 28.5	0	0	10% = 46,000	0

[1] In a case of pneumonia.

All forms of **leukæmia** are characterized by a conspicuous increase in the leucocyte count. In the early stages of these diseases, before such an increase in the white blood count has appeared, leukæmia may sometimes be suspected if there be a sudden increase in the leucocyte count, or if, in the stained preparation, there appear a preponderance of mononuclear leucocytes, i.e. myelocytes or lymphocytes. In leukæmia the red blood count and the hæmoglobin are often diminished. The excessive leucocytosis of leukæmia may sometimes be reduced by X-ray treatment. Leukæmias are divided as follows:

Lymphatic (lymphocytic) leukæmia in which an increase in **lymphocytes** goes hand in hand with enlargement of the lymph glands and hyperplasia of all lymphatic tissue. Many cases of lymphatic leukæmia run an acute febrile course, accompanied by a malignant hæmorrhagic diathesis similar to that of scurvy. In the acute cases there is a preponderance of the immature large lymphocytes and lymphoblasts. The bone marrow contains lymphocytes in enormous numbers almost to the exclusion of other forms (lymphoid transformation of the bone marrow). Spleen usually enlarged.

In **myeloid** (earlier spoken of as myelogenous) **leukæmia,** the spleen is greatly enlarged and the bone marrow usually altered. In the blood the number of premature leucocytes, particularly myeloblasts, myelocytes, and the forms intermediate between them and the polymorphonuclear leucocytes, is conspicuously increased. In addition, there appear myelocytes with eosinophilic granulation, and numerous nucleated red blood corpuscles. Occasionally there is an increase in the number of mast cells. In the bone marrow myelocytes and nucleated red blood corpuscles are found in enormous numbers and one may assume that these immature forms of the polymorphonuclear leucocytes and of the red blood corpuscles are washed out of the bone marrow into the blood stream. In myeloid leukæmia **Charcot-Leyden crystals** are sometimes found in the blood **postmortem** but never in the fresh blood examined during life.

Under the term **Pseudoleukæmia (aleukæmic leukæmia)** are grouped such cases as show either considerable enlargement of the lymph glands (as in lymphatic leukæmia), or a

striking enlargement of the spleen and liver (as in myeloid leukæmia), without the characteristic increase in the white blood count. The blood appears normal, or may show a slight reduction in the red blood count and hæmoglobin with a normal white count. Among the various disease pictures which have been grouped under the term pseudoleukæmia, one may differentiate the following:

Lymphatic pseudoleukæmia characterized by the presence of large masses of lymph glands in the neck, axillæ, and groin, and often accompanied by enlargement of the spleen. The glandular enlargement is produced by lymphoid hyperplasia. Occasionally lymphatic pseudoleukæmia may develop into genuine lymphatic leukæmia, in that the blood, which may for a long time have been normal or have shown only a relative preponderance of lymphocytes, may gradually or suddenly show a conspicuous increase in the lymphocyte count. It is assumed that this may be conditioned by the sudden discharge of lymphocytes from the lymph glands.

Malignant granuloma or **Hodgkin's disease** is characterized by swelling of the lymph glands, particularly those in the neck, and by splenomegaly. It is a chronic, and usually fatal, disease, in which the affected organs (lymph-glands, spleen and liver), are overgrown with lymphoid cells and with young connective tissue, so-called granulation tissue. This granulation tissue may later be transformed into fibrous connective tissue. The blood shows a progressive decrease in the number of red blood corpuscles as well as, often, a conspicuous reduction in the lymphocyte count. The eosinophilic leucocytes may be increased or decreased. The disease progresses, with periodic bouts of fever and positive diazo-reaction in the urine, and leads to death with severe anæmia and cachexia.

Lymphosarcoma or **lymphosarcomatosis** distinguished by the development of genuine sarcomatous tissue beginning in the lymph glands and spreading after the manner of a malignant tumor to involve the adajcent organs, e.g. in the mediastinum. The blood shows no characteristic alterations but the eosinophilic leucocytes are sometimes increased and the lymphocytes decreased.

Among a group of diseases which were earlier gathered under the term **splenic** pseudoleukæmia, and which may arise

Blood Picture in Infectious Diseases

Disease	W.B.C.	Eosinophiles	Lymphocytes	Remarks
Typhoid Paratyphoid	–	o	Relatively +	Blood platelets diminished.
Typhus	+			
Scarlatina	+	+		Punctate basophilia in severe cases.
Measles	–	– or o	Relatively –	Leucocytosis during incubation period.
Rubella	–	Normal	Relatively +	
Variola	+		+	Many large lymphocytes.
Varicella	Normal	Normal		
Diphtheria	+	–		Often myelocytes in children and, after serum, eosinophilia.
Angina (Vincent's)	+	Normal or –		
Erysipelas	+	o		
Acute Rheumatic fever	+ +	Normal, later +		Anæmia during convalescence.
Sepsis	+ (in severe cases –)	o	Relatively –	In later stages always anæmia (eventually polychromatophilic and nucleated erythrocytes).
Scurvy	Mononuclear leucocytes	–	Relatively +	Myelocytes 2–2.5%. During convalescence occasionally transient eosinophilia.
Trench Fever	+	+		Increase in large mononuclears.
Miliary Tuberculosis	Normal or –	o		
Influenza	Normal or –	– or o in severe cases		
Pneumonia	+	– or o		Blood platelets reduced at crisis; with empyema a rise in leucocyte count following crisis.
Pertussis	+	o	Relatively +	
Epidemic Meningitis	+	– or o		Fibrin +
Tuberculous Meningitis	Normal or slightly +	Normal		Fibrin –
Epidemic Parotitis	+		Lymphocytes and mononuclears +	

Blood Picture in Infectious Diseases (cont'd.)

Disease	W.B.C.	Eosinophiles	Lymphocytes	Remarks
Impetigo Contagiosa	+	+		
Plague	++			
Cholera	+			High leucocytosis = poor prognosis. R.B.C. sometimes increased due to anhydræmia.
Malaria	At onset of attack +. At height of fever −.	−at onset	During fever −. After fever in chronic forms considerably +.	Usually leucopænia persisting during course of the disease.
Relapsing Fever	−		Relatively +	Secondary anæmia.
Trichinosis	+	++	+	
Gas Gangrene	+	−	−	Myelocytes up to 1%. During convalescence a post-infectious lymphocytosis.
Pappataci Fever	−	−	+	Increase in eosinophiles = sign of convalescence.
Banti's Disease	−−			Relative increase in large mononuclears and transitionals. Secondary anæmia.
Weil's Disease	+		−at onset	Lymphocytosis develops during course of disease.
Tetanus	Neutrophilic leucocytosis			

under a variety of conditions, Banti's disease is particularly to be mentioned: Gradual progressive enlargement of the spleen and liver, finally ascites and cachexia. Blood not characteristic. Leucocytosis sometimes present, usually, however, there is a profound leucopænia with reduction of the eosinophiles. Wassermann reaction very often positive.

Certain instances of generalized infection characterized by ulcerative pharyngitis, and sometimes by more or less diffuse ulceration or gangrene of skin or mucous membranes, icterus and purpura, are associated with **"agranulocytosis"** —a conspicuous reduction of the total leucocyte count with almost complete disappearance of the cells of the myeloid series (granulocytes).

Acute mononucleosis is a febrile disease distinguished

by a lymphatic reaction. It frequently commences with sore throat; later the lymph glands (particularly those in the neck) and the spleen enlarge. The lymphocytes increase in the blood—up to 50,000 per cu. mm. and early forms of the lymphocytic series may appear. In some instances this disease may be distinguished from acute lymphatic leukæmia only by its course; acute mononucleosis is seldom fatal.

In the tables (page 170, and pages 173 to 174) are collected examples of the blood pictures in different blood and infectious diseases which indicate the diagnostic value of the differential white blood count. There are set down here not only the total leucocyte counts, but also the percentage of the different forms as well as the absolute numbers per cu. mm. It is to be noted that in infancy and childhood the lymphocytes compose a higher percentage of the total W.B.C. than in adults, e.g. during the first year of life 50%.

In the early stages of tuberculosis there is usually a relative increase in the lymphocytes in the presence of a normal leucocyte count. Eosinophilic leucocytes are present. In advanced cases there is frequently leucocytosis with a relative decrease in the lymphocyte count.

[The size and hæmoglobin content of red corpuscles in anæmia appear to vary according to the pathologic disturbance causing the anæmia. Upon this morphological basis all forms of anæmia may be divided into four groups: (1) macrocytic, (2) normocytic, (3) simple microcytic, and (4) hypochromic microcytic. In so far as ætiology is related to such changes rational therapeutic measures may go hand in hand with such a classification.

The volume and hæmoglobin content of the red corpuscles are most readily measured in the following way. Five cubic centimeters of blood are obtained from a vein and mixed with 10 mgm. of potassium oxalate. In the collection of the blood it is important that the syringe and needle be clean and dry in order that hæmolysis may be prevented. Congestion of the arm by the tourniquet should for obvious reasons be avoided. A definite proportion of potassium oxalate to blood is used because this substance causes shrinkage of the cells for which a correction must be made.

The blood so obtained is used for all quantitative determinations. Two red cell counts are made. These should check within 200,000 cells per c. mm. The hæmoglobin is accurately measured, in grams per 100 c.c. of blood. (Method of Sahli.) The volume of packed red cells is determined by means of an hæmatocrit. For this purpose the Wintrobe hæmatocrit is the simplest and most accurate clinical instrument. The hæmatocrit is filled to the 10 cm. mark and the blood is centrifugalized at 3,000 r.p.m. for 30 minutes (if packing is complete no further change in the volume of packed red cells should occur on further centrifugation). The height of the column of red cells measures the proportion of packed red cells in the blood. This reading should be multiplied by the factor 1.09 in order to correct for the shrinkage of the cells resulting from admixture of potassium oxalate.

From the data thus determined the mean volume and hæmoglobin content of the red corpuscles in the sample of blood, are calculated as follows:

Mean corpuscular volume (the average volume of the red cells, expressed in cubic microns) is the volume of packed red cells, expressed in c.c. per 1,000 c.c. of blood, divided by the number of red corpuscles, expressed in millions per c. mm.

Mean corpuscular hæmoglobin (the average **weight** of hæmoglobin in the red cells, expressed in micromicrograms) is the amount of hæmoglobin expressed in grams per 1,000 c.c. of blood, divided by the number of red corpuscles, expressed in millions per c. mm.

Mean corpuscular hæmoglobin concentration (the **concentration** of hæmoglobin in the red cells, expressed in per cent) is the amount of hæmoglobin, in grams per 1,000 c.c. of blood, divided by the volume of packed red cells, in c.c. per 1,000 c.c. of blood, multiplied by 100.

Example: R.B.C., 5.0 millions per c. mm., hæmoglobin 14.5 grams per 100 c.c. blood, volume packed red cells 44.0 c.c. per 100 c.c. blood; then,

$$\text{C.V.} = \frac{440}{5.0} = 88 \text{ cubic microns}$$

$$\text{C.H.} = \frac{145}{5.0} = 29 \text{ micromicrograms}$$

$$\text{C.C.} = \frac{145}{440} \times 100 = 33\%$$

Normal Blood Values (Adults)

	Males		Females	
	Average	Range of normal	Average	Range of normal
No. of red corpuscles millions per c.mm.	5.4	4.6–6.2	4.8	4.2–5.4
Hæmoglobin, grams per 100 c.c.	16.0	14–18	14.0	12–16
Volume packed red cells, c.c. per 100 c.c.	47.0	40–54	42.0	37–47

	Both Sexes	
	Average	Range of normal
Mean corpuscular volume (C. V.) cubic microns	87	82–92
Mean corpuscular hæmoglobin, (C. H.) micromicrograms	29	27–31
Mean corpuscular hæmoglobin concentration, (C. C.) per cent	34	32–36

Macrocytic anæmias are those in which the mean corpuscular volume is consistently found greater than normal.

Normocytic anæmias are those in which, in spite of even severe grades of anæmia, there is no significant alteration from the normal in the volume or hæmoglobin content of the red corpuscles.

Simple microcytic anæmias are those in which the mean corpuscular volume is less than normal while the mean corpuscular hæmoglobin concentration is normal or only slightly reduced (not less than 30%).

Hypochromic microcytic anæmias are those in which

the mean corpuscular hæmoglobin concentration is greatly reduced (to 29% or less). The volume of the red corpuscles is also reduced, often to a striking degree.

The magnitude of the above changes in the morphology of the red corpuscles depends to a large extent on the degree of anæmia. When the latter is slight, only minor changes occur. Obviously the blood examinations must be very accurately performed. Otherwise the calculations derived from them will be erroneous and misleading.

Macrocytic Anæmia: Castle and his associates have clearly demonstrated that for normal blood formation there is necessary an hæmatopoietic principle which is formed by the combination of an "intrinsic factor" (enzyme?) secreted by the gastric mucosa, and an "extrinsic factor" derived from the food and related to the vitamin B complex. The hæmatopoietic principle so formed is stored chiefly in the liver, but also in the kidney and other organs. When a break in the chain of metabolism of the hæmatopoietic principle occurs, macrocytic anæmia develops. Pernicious anæmia, the most common example of this type, is the result of defective secretion of "intrinsic factor." Such may also be the cause of the macrocytic anæmia encountered in rare cases of carcinoma of the stomach, following total gastrectomy, and in some instances of anæmia of pregnancy. The same type of anæmia may develop through lack of intrinsic factor in the diet, e.g., the tropical anæmia described by Wills; or through defective absorption of the combined "intrinsic" and "extrinsic" factors as may perhaps occur in some cases of celiac disease and in sprue. These anæmias are relieved by the administration of liver or liver extract. Macrocytic anæmia is also encountered in a proportion of cases of liver disease possibly as a result of faulty storage of hæmatopoietic principle.

Occasionally, moderate or slight macrocytosis is observed in cases of anæmia resulting from bone marrow disturbance (leukæmia, multiple myeloma, etc.) or in acute post-hæmorrhagic anæmia. This may occur with intense stimulation of the bone marrow and is probably due to the liberation of great numbers of reticulocytes into the blood stream. Immature erythrocytes are larger than adult forms.

Normocytic Anæmias. Such anæmia may result from (1) sudden blood loss; (2) acute blood destruction (e.g., malaria); and (3) lack of blood formation. In the latter group may be included not only aplastic anæmia, and the idiopathic form and that following poisoning by arsenic or benzol, but also the bone marrow aplasia associated with chronic inflammation and with tumors. The same type of anæmia is produced by replacement of bone marrow tissue by bone marrow tumors, both primary and metastatic, and by tumor-like growths such as in leukæmia.

In this type of anæmia, treatment is to be directed towards the removal of the cause. Transfusions may be required for supportive purposes.

Simple Microcytic Anæmias. A great variety of inflammatory and non-inflammatory diseases are associated with this type of anæmia. The depressing effect of such diseases on the bone marrow appears to lead to imperfect red cell formation. Treatment is directed towards the cause of the primary disease.

Hypochromic Microcytic Anæmia. This type of anæmia is encountered following long continued loss of blood, in hookworm disease, in chlorosis, in idiopathic hypochromic anæmia and following a diet defective in iron-containing foods. In these cases actual iron starvation seems to have resulted; such anæmia is relieved by the administration of large doses of iron. The therapeutic effect occurs even when the cause of the anæmia is still present. Such iron deficiency is associated with a greatly decreased mean corpuscular hæmoglobin concentration. M. M. W.]

MICROÖRGANISMS AND OTHER PARASITES OF THE BLOOD

To examine the blood for parasites of relapsing fever it is often sufficient to search through a fresh unstained preparation under high magnification. The spirochætæ are recognized by their motility. The plasmodia of malaria may also often be recognized in the fresh preparation. Or one may obtain a thick drop of blood on a slide, allow it to dry, place for 3–5 minutes in a solution of 1% acetic acid and 2% formalin, wash with distilled water and stain deeply with Giemsa's technique (1 drop in 2–4 c.c. water).

TABLE VI

CLASSIFICATION OF ANÆMIAS

Type of Anæmia	C. V. c. μ	C. C. %	Cause	Clinical Syndrome	Treatment
I. Macrocytic	>94	>30	(a) Lack of Castle's "Hæmatopoietic Principle"	(1) Pernicious Anæmia (2) Tropical anæmia of Wills (3) "Pernicious anæmia" of pregnancy (4) Rare cases of Carcinoma of stomach or other diseases of the stomach (5) Following total gastrectomy (6) Sprue (7) Macrocytic anæmia of celiac disease (8) Macrocytic anæmia of liver disease (9) Rarely, pellagra	Liver, or liver extract
			(b) Intense bone marrow stimulation	In conditions usually associated with normocytic anæmia	Treatment of cause Transfusions
II. Normocytic	80–94	>30	(a) Sudden Blood Loss	Acute Post-hæmorrhagic anæmia	Treatment of cause Transfusions
			(b) Acute Blood Destruction	e.g., Hæmolytic anæmia of malaria	
			(c) Lack of Blood Formation	(1) Aplastic Anæmia (idiopathic and secondary) (2) Bone marrow tumors; also leukæmia (3) Chronic inflammatory and non-inflammatory diseases	Attempts to stimulate blood formation, as by arsenic
			(d) Hydræmia	"Physiologic anæmia" of pregnancy	
III. Simple Microcytic	<80	>30	Imperfect Blood Formation	Subacute and chronic inflammatory diseases and chronic non-inflammatory conditions	Treatment of cause Transfusions
IV. Hypochromic Microcytic	<80	>30	Deficiency of Iron through (a) Loss of Blood	(1) Chronic post-hæmorrhagic Anæmia (2) Hookworm Anæmia	Iron (inorganic) in large doses
			(b) Defective Absorption by G. I. tract	Idiopathic Hypochromic Anæmia	
			(c) Deficiency in diet	Diet deficient in iron	
			(d) Undetermined	Chlorosis	

To identify staphylococci and streptococci as well as colon bacilli which may appear in the blood in severe sepsis, in puerperal fever, and with endocarditis, or the bacillus of gas gangrene, or pneumococci which may overflow into the blood in severe pneumonia, or typhoid bacilli, commonly present in the blood during the first week of the disease, several c.c. of blood are withdrawn from the cubital vein with a sterilized fine needle, after thorough cleaning of the skin. The blood so obtained is placed in several tubes with sterile nutrient bouillon. If bacterial growth, evidenced by clouding, takes place in these tubes a transplant is made with a platinum loop upon solid media and the exact identification of the bacteria is carried out. Or blood obtained by venapuncture may be mixed directly in a tube with fluid agar and a plate poured in a Petri dish. More exact details regarding bacteriological examination and serum reactions are described in the chapter on Microörganisms.

The demonstration of parasites in the blood, e.g. trichina embryos, trypanosomes, spirochætæ, malaria plasmodia, etc., may be accomplished by the method of Staubli. One c.c. or more of blood is withdrawn by venapuncture, diluted with several volumes of 1% acetic acid, and, after hæmolysis is complete, the mixture is centrifuged. The sediment is withdrawn with a pipette, spread upon a slide, fixed with absolute methyl alcohol and stained with Jenner-May or Giemsa stain.

PERSONAL NOTES

PERSONAL NOTES

CHAPTER V

URINARY SYSTEM

ANATOMICAL CONSIDERATIONS

THE **kidneys** lie on either side of the spine at the level of the twelfth thoracic and first to the third lumbar vertebræ. The right kidney lies immediately below the liver; the left just under the spleen. By percussion one determines first the lower border of the liver and spleen and finally the lower boundary of the kidney percussing upward from the ilium. The lower pole of the kidney lies normally about 10 cm. lateral to the spinous process of the vertebræ. Below the renal dulness one obtains a tympanitic percussion note over the lumbar vertebræ and sacrum, while over the vertebræ in the region of the kidneys, spleen or liver, the note is distinctly dull.

Reduction in size of the kidney, e.g. contracted kidney, cannot be demonstrated by percussion. It is, however, sometimes possible to demonstrate absence of the kidney dulness when one kidney has been removed. Percussion is often of significance in the diagnosis of tumors of the kidneys and hydronephrosis. Large tumors of the kidney tend to push the colon forward and inward.

The kidneys normally move up and down with respiration. If enlarged by tumors, the respiratory excursion of the kidney is less than that of the liver or spleen. If the kidney be pushed well downward by deep inspiration, the palpating hands may sometimes hold it in that position during expiration.

A so-called "floating kidney," which occurs much more frequently on the right side than on the left, may descend so far downward that at the end of a deep inspiration it is palpable as a smooth round tumor, below the liver or spleen. With one hand posteriorly in the lumbar region one may feel the kidney slide back into its old position with expiration. Descent of the kidney is usually combined with gastroptosis and enteroptosis (Glenard's disease).

The **prostate** can be palpated with the examining finger in the rectum as a firm organ about 3–4 cm. in diameter. It is atrophic in all cases of hypogenitalism, e.g., in cases of malformation or insufficient development of the testicles. Enlargement of the prostate, to the size of an apple, may occur in older men, and may lead to dysuria or to complete urinary retention. This hypertrophy may not involve the entire gland but only the middle lobe; this may protrude so as to occlude the vesical orifice. With inflammation of the prostate the examining finger in the rectum may press out a thick, sometimes purulent, secretion through the urethra. Prostatic abscess renders the gland very painful to palpation; with carcinoma of the prostate the nodular gland becomes hard as stone and frequently a somewhat bloody secretion is exuded through the urethra.

When the **urinary bladder** is distended by from 300–500 c.c. fluid there develops a sensation of pressure and a desire to void. Painful urination, often associated with abnormally frequent micturition (polyuria), occurs with cystitis, also with the "irritable bladder" of nervous individuals, and especially with vesical tuberculosis, which often leads eventually to chronic contraction of the bladder.

The urinary bladder may be percussed and sometimes felt, when considerably distended, as a round swelling in the midline just above the symphysis. Conspicuous distention of the urinary bladder occurs chiefly with obstruction of the lower urinary passages by a stone, cicatricial stricture, or enlargement of the prostate, during parturition, in unconscious patients, and finally in certain diseases of the spinal cord which lead to paralysis of the nerve supply of the bladder. Under these latter conditions, in spite of the fact that the over-filled bladder may not be voluntarily emptied, the urine may be passed involuntarily from time to time in small amounts (so-called paradoxical incontinence).

Obstruction at or below the vesical orifice leads to hypertrophy and trabeculation of the bladder musculature. In some instances the bladder, in spite of the hypertrophy of its musculature, can not be completely evacuated voluntarily; there remains at the completion of micturition a considerable amount of "residual urine." This may be measured

by catheterization immediately following voluntary micturition and serves as an estimate of the degree of insufficiency of the bladder.

A vesical calculus may cause sudden interruption of the urinary stream during micturition by occluding the internal vesical orifice. It may also lead to hæmaturia; under these circumstances the urine is most bloody toward the end of the act of micturition.

Renal colic is characterized by paroxysmal attacks of severe pain arising in the flank or in the region of the kidney and radiating downward into the groin or testis. X-ray examination in such instances may disclose the shadow of a calculus in kidney pelvis or ureter.

Recently, following intravenous injection of 20 c.c. of a very stable iodine compound ("neoiopax") visualization of the kidneys and urinary passages has been accomplished by means of X-ray (intravenous pyelography). This solution is excreted in healthy individuals within 5 to 20 minutes in such concentration that the urine in the kidney pelves, ureters and bladder is opaque to X-ray. It is thus possible to discern diagnostically significant displacements, or deformity of these organs without resorting to cystoscopy. In cases of damage to the kidney parenchyma the excretion of the substance is delayed so that visualization of the urinary tract by X-ray may only be possible hours after the injection.

THE URINE

The products of the breakdown of fat and carbohydrates leave the body, usually in the form of carbon dioxide and water, through the **lungs.** The end-products of **protein metabolism,** on the other hand, are excreted almost exclusively through the **urine.** Careful examination of the urine, therefore, makes it possible to follow, qualitatively and quantitatively, the metabolism of protein in the organism. In addition the examination of the urine may give important information concerning disturbances of metabolism, as well as regarding disease of the kidney or urinary passages, and even with regard to functional abnormalities of the liver, or of the heart and circulation.

The examination of the urine should include the follow-

ing: The volume excreted per day, the specific gravity, the color and reaction. In addition it should be tested for the presence of albumin and sugar (cloudy urine must be filtered before these tests are made). Urine which contains pus cells or bacteria is usually turbid, and sometimes cannot be cleared by filtration. Under these conditions it must be shaken with kaolin and then filtered. According to its color the urine should be tested for the presence of bile pigments, blood pigments, urobilin and porphyrin. Finally the urinary sediment should be examined microscopically. In certain cases the examination must include tests for other substances (e.g. in diabetes for acetone and diacetic acid), and the quantitative estimation of albumin, sugar, nitrogen, etc.

The normal male voids approximately 1500 to 2000 c.c. per day, and the female 1000 to 1500 c.c. A daily volume of less than 500 or over 2000 c.c. is usually to be regarded as abnormal.

Persistent **increase in the volume output of urine (polyuria)** occurs most conspicuously (up to 9–20 liters) with diabetes insipidus and with polydipsia, to a lesser degree (3–5 liters) in diabetes mellitus, with certain types of nephritis (contracted kidney), with prostatic hypertrophy, with pyelitis, and finally with absorption of œdema, pleural and peritoneal effusions. **Reduction of the urinary volume** (**oliguria**) occurs in fever, in certain acute and chronic diseases of the kidney (nephritis with œdema), in severe diarrhœa, e.g. in cholera, with profuse sweating, during the accumulation of exudates and transudates, and finally with impairment of blood-flow through the kidney (circulatory failure and ascites).

Polyuria and oliguria are not to be confused with **pollakiuria** (frequent) and **olikaguria** (seldom). By pollakiuria is understood a condition in which the patient is compelled to urinate very frequently, sometimes as often as every half hour, e.g. in cystitis or with so-called irritable bladder. In olikaguria the bladder is emptied only at long intervals, once to three times a day (e.g. in tabes). Difficult or painful urination is described as **dysuria.**

By **oligodipsia** is understood a pathologically small, and by **polydipsia** a pathologically increased demand for fluid.

The former leads to a decrease, and the latter to an increase in the urinary output.

While in the normal individual the urine is secreted principally during the day and only a small quantity at night, it is often observed in patients with heart disease, pyelitis, or vascular disease of the kidney, that a far larger amount of urine is secreted during the night (nycturia).

The **specific gravity** is measured by dipping a dry hydrometer into the urine cooled to room temperature; the hydrometer is read at the lower level of the fluid meniscus. The specific gravity is dependent upon the amount and the **weight** of the dissolved substances.

The specific gravity of the urine ranges normally between wide limits, approximately 1.003 to 1.040. With increased fluid intake large quantities of urine of low specific gravity are excreted; upon a small fluid intake or with a considerable loss of water in the form of perspiration during vigorous exercise, or via the bowel in diarrhœa, small quantities of urine are passed having a high specific gravity. It is characteristic of the healthy kidney that it adapts quickly and perfectly to such changing conditions and that despite the alterations in the volume of urine secreted the elimination of salts and of the products of metabolism goes on unimpaired. Considerable variations in specific gravity and therewith in the concentration of the urine are to be noted if each specimen passed in the course of 24 hours be examined separately. If, on the other hand, the total 24-hour urine be collected and mixed these variations in concentration are less apparent; specific gravity of the **total** urine of the healthy individual varies only between 1.015 and 1.030 from day to day.

In certain forms of nephritis, acute and chronic, and particularly with the so-called "contracted kidney," the kidneys have apparently lost the ability to meet the changing conditions of fluid balance; following an increase in the fluid intake little or no increase and dilution of the urine may take place, or such occurs only after considerable time. Most striking, however, is the inability of such a diseased kidney to secrete concentrated urine rich in salts and in the products of metabolism; these substances may only be excreted in considerable dilution (**hyposthenuria**). In many

severe cases of diffuse nephritis there is secreted, even under the most variable conditions, urine of low fixed specific gravity, about 1.010 (**isosthenuria**). If the **total volume** of such dilute urine is large, as is often the case with the contracted kidney, the elimination of the metabolic products may be adequate. If, on the other hand, as so often happens in acute nephritis and in certain forms of chronic nephritis, the total urinary volume is small, the elimination of water as well as that of metabolites is insufficient. Under these circumstances renal insufficiency or even uræmia may develop.

Not only in the nephritides are such urinary changes noted. Polyuria and hyposthenuria may occur with pyelitis, with urinary obstruction resulting from prostatic hypertrophy, and in diabetes insipidus (1.012 to 1.001). Large amounts of urine of high specific gravity (1.030 to 1.050) are excreted in diabetes mellitus; the passage of small amounts of urine of high specific gravity is characteristic of fever and congestive circulatory failure.

From the specific gravity of the urine the total concentration of solids in grams may be calculated by multiplying the last two figures of the specific gravity by Hæser's coefficient, 2.3. For example, a urine of specific gravity 1.015 (15×2.3) contains 34.5 grams solids per liter, which, with a total urinary volume of 2000 c.c., represents the elimination of 69.0 grams of solids per day.

The **color of the urine,** which is normally yellow, is fainter with a more dilute urine, and darker, a more reddish yellow, if the urine is more concentrated. Bright yellow urine of high specific gravity is often found with diabetes mellitus. The urine is a dark, yellow-brown (the color of beer) and has a yellow foam if bilirubin be present, i.e. with icterus; reddish-yellow or reddish-brown if it contain urobilin, a reddish-wine color with porphyrinuria, a smoky red, i.e. red and at the same time slightly cloudy and iridescent, if blood be present therein. The original normal color of the urine deepens somewhat upon standing in air and may change to a greenish-brown following the use of phenol, lysol, naphthol, hydroquinone, salol, or with alkaptonuria or melanuria.

The **reaction** of the normal, freshly voided, human urine is acid, principally due to the presence of diacid sodium

phosphate. Occasionally the reaction of the normal urine may be neutral, changing blue litmus faintly red, and red faintly blue. This is the case if large quantities of the dibasic phosphates are present together with diacid phosphates. When only the dibasic phosphates, or with these, tribasic phosphates are present the reaction is alkaline (see page 201).

Reaction is more **strongly acid** if the urine is highly concentrated, e.g. after profuse perspiration, or when the protein metabolism of the organism is stimulated (e.g. in fever and upon a high meat diet), since the sulphur of the protein and the phosphorus of the nuclein and lecithin, in the process of metabolism appears as sulphuric or phosphoric acid in the urine. The reaction of the urine may be **less acid, neutral,** or even **alkaline,** if, as a result of persistent vomiting or following repeated gastric lavage, large quantities of HCl are removed from the stomach; also shortly after the heavier meal, and on a vegetable diet. The acetic, tartaric, citric and vegetable alkalies, which are abundant in fruit and vegetables, are metabolized in the organism to carbonates, which render the urine alkaline. During the absorption of exudates and transudates the reaction of the urine may be less acid since the alkali contained in these (always alkaline) fluids goes over into the urine; during the accumulation of exudates, on the other hand, the urine may be more acid.

If the urine be extremely acid, that is if it contain diacid phosphates, uric acid may be liberated from the urates and precipitates in the form of whetstone-shaped crystals. The acid reaction of the urine may be titrated with N/10 solution of alkali against phenolphthalein as an indicator, or more simply determined by the procedure of Neubauer, which consists in mixing the urine in a flask with several c.c. of a solution of lackmoid in ether. Normally acid urine takes on, under these circumstances, a faint blue or green color; hyperacid urine, on the other hand, remains colorless, and alkaline urine removes the reddish dye from the solution and becomes a deep blue. The lackmoid solution is prepared by mixing a few grains of the dye in several c.c. of alcohol, dissolving by heating over a water bath, adding 300 c.c. of ether and filtering.

As soon as the urine becomes neutral or alkaline the

phosphates are precipitated (dibasic or tribasic calcium and magnesium phosphates, as well as the carbonates of the alkaline earths) producing a white flocculent precipitate. The urine is sometimes clouded with these salts at the time of voiding. Weakly-acid or a neutral urine becomes cloudy upon heating due to the precipitation of phosphates. This precipitate may be dissolved by the addition of acetic acid, in contrast with the precipitate of albumin which forms upon heating. It persists after the addition of alkali. A precipitate of urates, present sometimes in an acid urine may be dissolved by heat or by the addition of potassium or sodium hydroxide. This powdery sediment of urates is usually, but not always, brick red.

If, through the action of bacteria, decomposition of the urine takes place in the bladder, or in the pelvis of the kidney (with cystitis or pyelitis), or after voiding, ammonium carbonate is formed from the urea and the reaction of the urine becomes alkaline (ammoniacal fermentation). Ammoniacal urine has a sickening odor and if a rod dipped in HCl is held over it there forms a mist of ammonium chloride. While crystals of ammonium-magnesium phosphate occasionally appear in sediment of the urine which has not undergone alkaline decomposition, in the presence of ammoniacal fermentation these coffin-shaped crystals form in large numbers and are often accompanied by the thorn-apple forms of ammonium urate. The blue color formed by placing a drop of ammoniacal urine on litmus paper disappears when the paper is dried in air. Pus in the urinary sediment accumulates in flakes in an acid urine, while in an alkaline, decomposing urine it forms mucoid, tenacious clumps.

URINARY CONSTITUENTS

Organic Constituents

Urea $CO(NH_2)_2$ is very easily soluble in water and alcohol. The daily output in health is from 20 to 40 gms.; it is increased upon a high protein diet, as well as by the destruction of the body protein in fever (up to 60 gms.), and decreased in inanition (as low as 9 gms.), upon any nitrogen-poor or carbohydrate-rich diet, and in many forms of nephritis.

Urea is broken down by the action of certain bacteria or by alkalis, and, taking up water, forms ammonium carbonate:

$$\begin{matrix} NH_2 \diagdown \\ \quad\;\; C{:}O \\ NH_2 \diagup \end{matrix} + 2H_2O = \begin{matrix} NH^4O \diagdown \\ \qquad\;\; C{:}O \\ NH^4O \diagup \end{matrix}$$

Urea heated without the addition of water forms biuret, an aqueous solution of which gives a violet color when treated with potassium hydroxide and a drop of very dilute copper sulphate (**biuret reaction).**

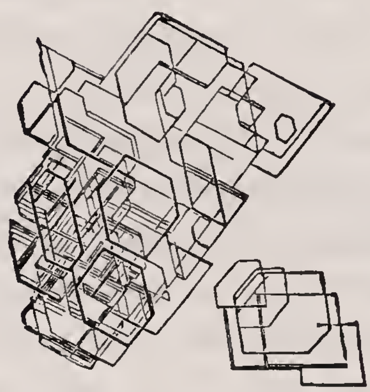


FIG. 53.—Urea nitrate.

Since urea is a normal constituent of the urine the qualitative demonstration of its presence here is of no importance, but only in such excretæ as do not normally contain urea, e.g. in the vomitus or sputum of uræmic patients. The fluid to be examined is evaporated to dryness; the residue is dissolved in alcohol and filtered; the filtrate reëvaporated, the residue from this evaporation dissolved in water and treated with concentrated nitric acid. After standing in the cold crystals of urea nitrate form in sheets (Fig. 53).

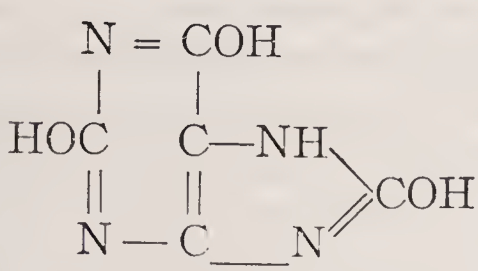
Quantitative Determination of Urea or Urea Nitrogen

The nitrogen appearing in the urine is excreted principally (about 80%) in the form of urea. A not inconsiderable amount of nitrogen is, however, present in other combinations, e.g. uric acid, creatinine, etc. and it is therefore more advisable, in order to gain information concerning the nitrogen metabolism, to determine the **total nitrogen** of the urine. Quantitative determination of the urinary nitrogen is most accurately made by the Kjeldahl method:

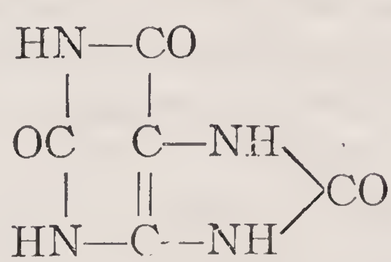
Five c.c. of urine are mixed with 10 c.c. of pure, concentrated sulphuric acid, several crystals of copper sulphate, and 3 to 4 gms. of potassium sulphate in a long-necked flask of hard glass, and the mixture is boiled until the fluid is entirely clear. After cooling it is diluted with water and treated with 50 c.c. of concentrated sodium hydroxide; the ammonia formed by this procedure is distilled off into another vessel filled with a known amount (50 to 100 c.c.) of N/10 HCl. After complete distillation the acid is titrated to neutrality against a few drops of methyl red: red to yellow. The quantity of N/10 acid in c.c., which has been neutralized by the ammonia distilled from the mixture, represents, upon multiplying by 1.4, the amount of nitrogen in mgm. contained in the 5 c.c. specimen of urine. In determining the non-protein nitrogen in the blood smaller amounts of N/100 acid and N/100 alkali are used, corresponding to the smaller amounts of nitrogen, and, in place of the titration with sodium hydroxide, the iodometric titration of Bang may be employed.

In all quantitative determinations of the urinary constituents it is particularly necessary to collect and to measure accurately the total daily output. For example if the urinary output be 1500 c.c. per day and the nitrogen content 1.2%, it is evident that the nitrogen excretion is 18 gms. per day.

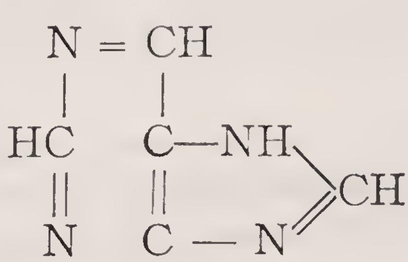
Uric Acid ($C_5H_4N_4O_3$) = trioxypurine



or



and the xanthin or alloxur bases, to which belong xanthin = dioxypurine ($C_5H_4H_4O_2$), hypoxanthin ($C_5H_4N_4O$), guanin ($C_5H_5N_5O$) and adenin ($C_5H_5N_5$) are derived from purine:



and are grouped under the term "Purine bodies." (See chapter on Metabolism.)

With regard to the derivation of uric acid from the nucleo-protein as well as its relation to normal and pathological conditions, e.g., gout, see the chapter on metabolism and nutrition.

The daily output of uric acid in the normal individual is from 0.2 to 1.0 gms., depending upon the type of the food (see chapter on Metabolism and Nutrition). It is raised in all diseases in which increased destruction of cell nuclei takes place, i.e. in pneumonia in the stage of resolution, and in leukæmia.

Uric acid is a dibasic acid and as such forms two series of salts (urates): the dibasic urates, e.g. $Na_2(C_5H_2N_4O_3)$

Comb form Whetstone form

FIG. 54.—Uric acid crystals.

di-sodium urates, which exist only in solutions far more alkaline than exist in the human body or its secretions, and the mono-acid urates, e.g. $NaH(C_5H_2N_4O_3)$ mono-sodium urates. Uric acid occurs in this form in the blood and body fluids, and in needle-like crystals of this compound in the concretions of gout, e.g., tophi. In addition to the mono-sodium urates there occur in the urine other more acid salts, compounds of one molecule of the mono-acid urate with one molecule of free uric acid, e.g. $NaH(C_5H_2N_4O_3)—H_2(C_5H_2N_4O_3)$ hemi-sodium urate, so-called, since two molecules of uric acid are combined with a single atom of sodium. Whether this acid sodium urate exists as a genuine chemical compound or is simply a mixture of sodium urate with uric acid has yet to be demonstrated.

Uric acid is dissolved in the urine principally in the form of its salts (mono-sodium and hemi-sodium urate) but in part also as free uric acid. In concentrated and very acid urines

(in fever, after profuse perspiration) hemi-sodium urate precipitates, after standing in the cold, in the form of amorphous, usually reddish-yellow, brick-dust-like sediment which upon warming or upon the addition of alkali goes back into solution. **Free uric acid,** almost insoluble in water, appears in any strongly acid urine, particularly after standing. It forms a heavy precipitate upon the bottom of the specimen glass, composed of reddish-yellow sand, which shows microscopically, whetstone-, comb-, and sphere-shaped crystals (soluble in potassium hydroxide). Under certain conditions uric acid may crystallize out in the pelvis of the kidney or in the bladder leading to the formation of stones which may in turn give rise to localized bleeding. In decomposing urines the uric acid combines with the ammonia. Ammonium urate is only

FIG. 55.
Sodium urate—amorphous sediment.

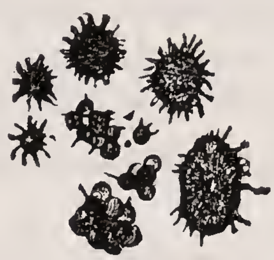


FIG. 56.
Ammonium urate—Thorn-apple form.

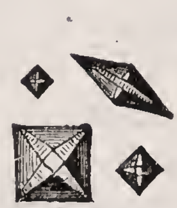


FIG. 57.
Calcium oxalate—envelope form.

slightly soluble and appears in the sediment in the form of thorn-apple crystals (see Fig. 56).

The **qualitative demonstration of uric acid** comes into consideration in the examination of urinary sediments, of the gouty concretions, and of renal stones. A small portion of the specimen to be examined is dissolved in the porcelain dish with a few drops of nitric acid, and the solution slowly evaporated; small orange-red flecks form on the dish, which give a purple color when moistened with ammonia, or turn blue after the addition of potassium hydroxide (murexide test).

Quantitative estimation of uric acid in urine (Folin-Schaffer method). The uric acid is precipitated as ammonium urate by the addition of ammonia. Titration with permanganate.

Reagents: I. 500 gm. ammonium sulphate, 5 gm. uranium acetate, and 60 c.c. of 10% acetic acid dissolved in 1 liter.

II. A 10% solution of ammonium sulphate. III. Concentrated sulphuric acid. IV. 25% ammonium hydroxide. V. N/50 potassium permanganate.

Method: Sixty c.c. urine are mixed in a graduated cylinder with 15 c.c. solution I, and after the precipitate has formed the mixture is filtered. Into each of two centrifuge tubes are pipetted 25 c.c. filtrate, mixed with 2 c.c. of IV, and allowed to stand overnight. The precipitate is thrown down in a centrifuge, washed with 15 c.c. II, and re-centrifuged. Fifteen c.c. water and 3 c.c. III are added to the precipitate which dissolves upon warming. This solution is then titrated with V to a purple color.

Calculation: c.c. permanganate $\times$ 1.5 = uric acid in 25 c.c. filtrate = 20 c.c. urine.

Microchemical Colorimetric Method (Folin-Wu). The principle of the method depends upon the fact that uric acid gives, with phosphotungstic acid and alkali, a deep blue color the depth of which is proportional to the amount of uric acid present.

Reagents: I. Uric acid reagent: Transfer 100 gm. sodium tungstate to a 2 liter flask and add 750 c.c. of distilled water. Shake until dissolved. A little white precipitate of calcium may remain. Add 80 c.c. of 75% phosphoric acid. Close mouth of flask with a funnel and 2 watch glasses, one small and one large, and boil gently but continuously for 2 hours. If very dark in color bleach with a few drops of bromine and boil for 10–15 minutes to remove excess. Cool and dilute to 1 liter.

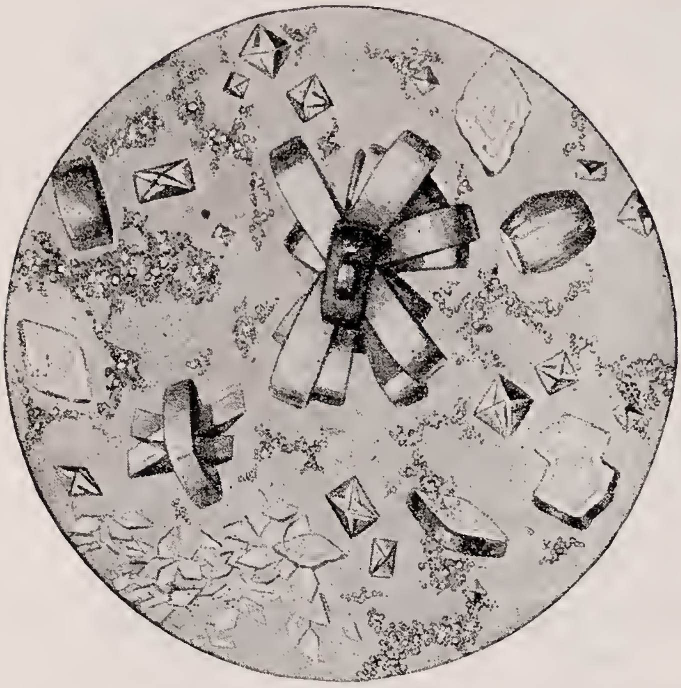
Method: Transfer 2–5 c.c. of urine and about 3 c.c. of water to a centrifuge tube. Add 3 c.c. of clear acid silver lactate (5 gm. silver lactate, 5 c.c. lactic acid and 5 c.c. 10% NaOH) and centrifuge for 2 to 3 minutes. Add a drop of silver lactate solution to the supernatant fluid. If a precipitate forms too much urine has been used. Repeat using smaller amount. If no precipitate forms pour off supernatant fluid as completely as possible. To a 100 c.c. volumetric flask transfer 5 c.c. of standard uric acid solution (10 c.c. of stock solution, diluted to 100 c.c.) containing 0.5 mg. uric acid. Add to the standard from a burette 2 c.c. of 15% sodium cyanide and add the same amount to the precipitate in the centrifuge tube.

Stir the latter to complete solution, then rinse into a 100 c.c. flask using 20 c.c. of 20% sodium carbonate solution from a cylinder and add 5 c.c. of water to balance that in standard. Add 20 c.c. of sodium carbonate to standard and then, with shaking, 5 c.c. of the uric acid reagent I to each flask. Let stand for 5 minutes. Then shake for a few seconds, dilute to mark with water and shake vigorously for a few seconds more. After mixing, pour out (or into test tubes) about 40 c.c. from each flask. This facilitates settling of the precipitate which is a decomposition product of excess uric acid reagent. Pour off clear supernatant fluids into colorimeter cups and compare. The cyanide and the prussic acid formed from it in acid solution are very poisonous. Pour all discarded solutions directly into drain pipes.

Oxalic acid $\begin{array}{l} COOH \\ | \\ COOH \end{array}$, daily output about 0.02 gm., appears in the sediment as calcium oxalate (insoluble in acetic acid, soluble in hydrochloric acid) in strongly refractile octahædral crystals, (see Fig. 57), more rarely in needle or biscuit-shape. Neither the qualitative nor quantitative demonstration of oxalic acid is of diagnostic significance, except in so far as the persistence of "oxaluria" may predispose to the formation of calculi.

Creatinine ($C_4H_7N_3O$), daily output 0.6–1.0 gm. increases with increased muscular activity, decreases with inanition and during convalescence. Creatinine in the urine gives a deep red color upon the addition of a few drops of a freshly prepared solution of sodium nitroprusside and a few drops of sodium hydroxide (see Legal's test for acetone, Page 221).

Quantitative determination of creatinine by Folin's method is as follows: 0.5 c.c. of urine is placed in a 100 c.c. measuring glass, 1.5 c.c. of a 1.2% picric acid solution and 0.5 c.c. of a 10% sodium hydroxide solution are added, the mixture is shaken, allowed to stand 5 minutes and diluted to 100 c.c. with distilled water. The solution is then examined colorimetrically in comparison with a 0.981% solution of potassium bichromate. The test is repeated with varying amounts of urine in order to obtain a reading between 40 and



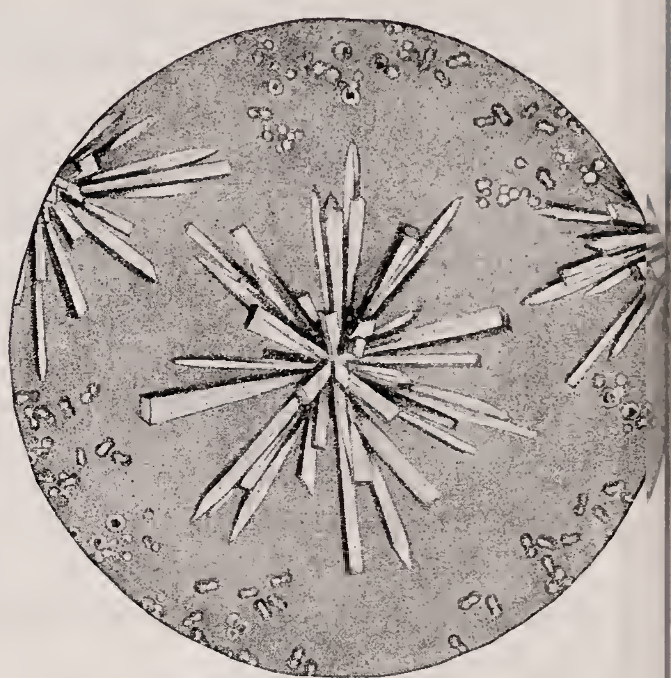


Fig. 57a.—Sediment from acid urine: whetstone and barrel-shaped crystals of uric acid; acid sodium urates in granules; envelope-shaped crystals of calcium oxalate.

Fig. 57b.—Crystals of calcium (monacid) phosphate together with ball and biscuit forms of calcium carbonate.

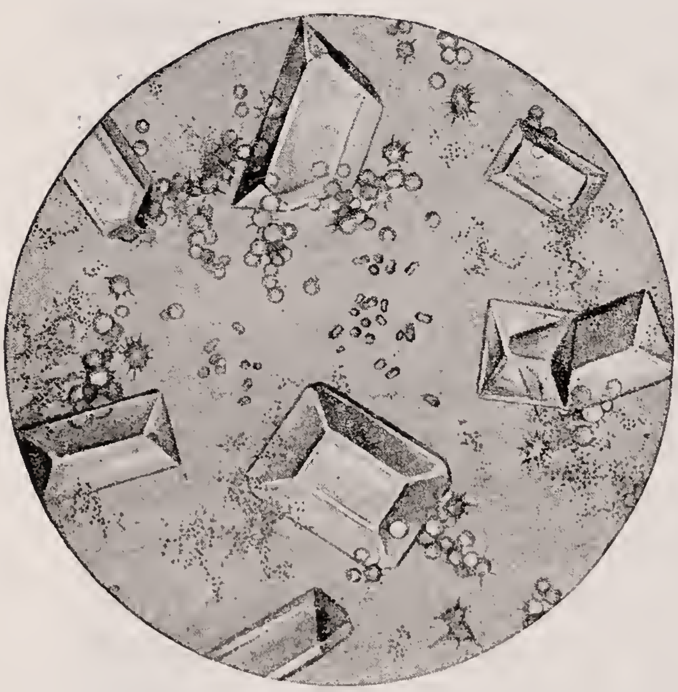
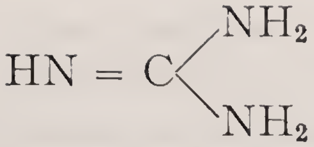


Fig. 57c.—Sediment from urine which has undergone ammoniacal degeneration: coffin-lid crystals of ammonium-magnesium phosphate, and thorn-apple forms of ammonium urate.

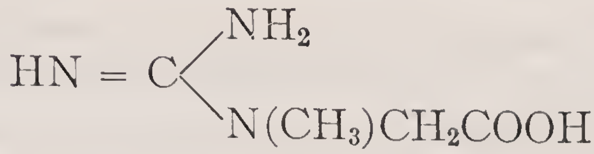
Fig 57d.—Crystals of tyrosine, and leucine, in urinary sediment.

60 on the scale of Autenrieth's colorimeter. (See page 138 and **Neubauer,** Münch. Med. Wochnschr. 1914, 857.)

Creatine appears in small quantities in the urine and its formula indicates its derivation from guanidine:

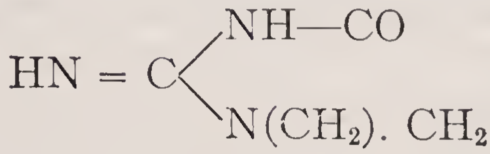


Guanidine.



Creatine.

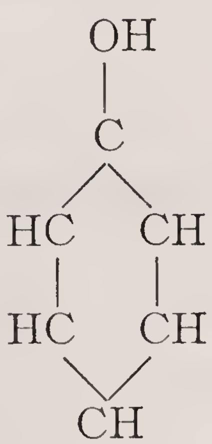
(Methylguanidine acetic acid)



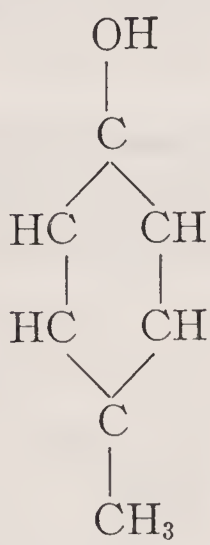
Creatinine.

Hippuric acid ($C_9H_9NO_3$), daily output 0.1 to 1.0 gm., is synthesized in the kidney from benzoic acid and glycocoll and appears occasionally in the sediment in needles or rhomboid prisms which are similar to the crystals of the triple phosphates but are insoluble in acetic acid.

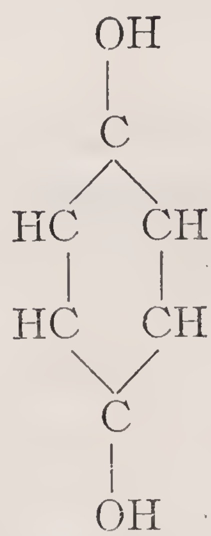
Phenols: Phenol (C_6H_5OH = carbolic acid); cresol ($CH_3C_6H_4OH$); hydroquinone $C_6H_4(OH)_2$.



Phenol.



Cresol.

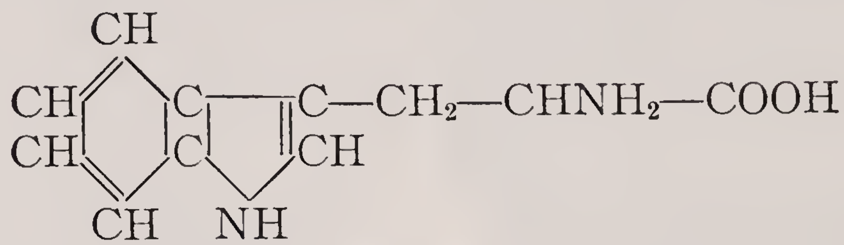


Hydroquinone.

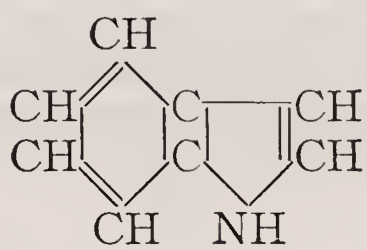
Phenol appears in small quantities in the normal urine bound to sulphuric acid, as a so-called ethereal sulphate, e.g., phenol-sulphuric acid. An increase of this compound indicates putrefaction in the organism since phenol is formed by this process from tyrosine. In addition phenol may appear in the urine in large quantities if carbolic acid or similar substances are absorbed from the stomach, the skin, or body cavities, e.g., with attempted poisoning with carbolic acid or lysol (lysol is a solution of cresol in soap). Urine containing phenol darkens on exposure to the air. To test for phenol in the urine 100 c.c.

are treated with 5 c.c. of concentrated sulphuric acid and distilled. In the distillate the presence of phenol may be demonstrated by the production of a pale yellow precipitate of tribromphenol upon the addition of bromine water.

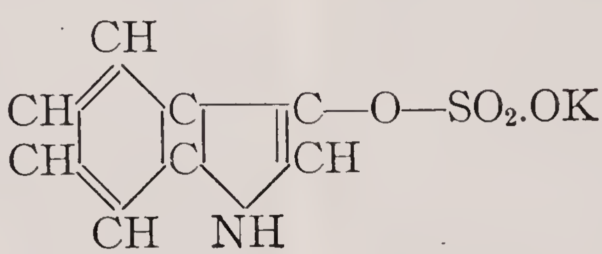
Indican (potassium indoxylsulphate): From the tryptophane = indolaminopropionic acid, of the proteins.



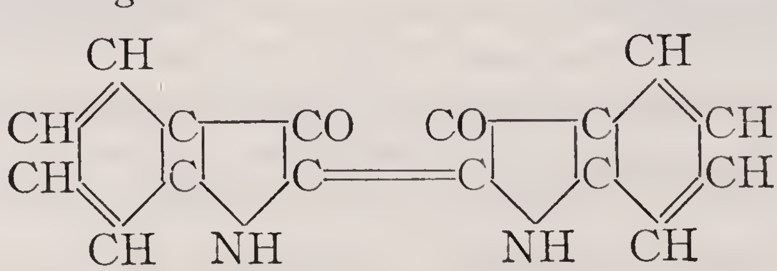
is formed by putrefaction in the intestinal canal, or in putrid suppuration, indol:



Indol is absorbed from the intestinal canal, oxidized in the body to indoxyl, and excreted in the urine combined with sulphuric acid as indoxylsulphate of potassium.



This compound breaks down upon treatment with HCl to form indoxyl, which upon oxidation (e.g., with chlorinated lime) forms indigo:



Indican is increased in intestinal diseases with abnormal putrefaction of the intestinal contents, in cholera, peritonitis, and most strikingly in intestinal obstruction. From the

amount of indican in the urine one may judge the intensity of the protein putrefaction in the intestinal canal.

To **test for indican** 10 c.c. of urine are treated with about 10 drops of a 10 % solution of lead acetate, whereby a number of confusing substances are thrown down, and the precipitate is filtered off. Six c.c. of a solution containing 0.1 gm. ferric chloride in 50 c.c. concentrated HCl are now added. A few c.c. of chloroform are then added and the indigo dissolved out by shaking.

Sometimes in place of the blue color of indigo blue there appears a red or violet tint, particularly if the urine is treated with concentrated nitric acid (instead of with HCl and chlorinated lime) and is heated, and if one extract with ether instead of with chloroform. This "indigo red" probably arises from indoxyl sulphuric acid, and hence from indol, and has no other significance than that of indigo blue. Some urines become pink upon the addition of sulphuric acid. The formation of this color (urorosein) depends upon the presence of indol-acetic acid.

Inorganic Constituents

Hydrochloric acid, HCl, appears in the urine principally combined with sodium as sodium chloride. The daily output of sodium chloride is normally about half that of the urea, between 6 and 15 gm.; it is dependent principally upon the amount of salt in the food.

The excretion of sodium chloride is decreased in inanition and in fever, particularly in pneumonia; in the latter chloride excretion may be so reduced that, upon the addition of silver nitrate to the urine acidulated with nitric acid, there appears only a faint cloudiness, while normally, with a content of about 1 % in the urine, the addition of silver nitrate and nitric acid throws down silver chloride in large masses.

The excretion of chlorides is also diminished (from 5 to 1 gm.) during the accumulation of transudates or œdema, particularly during the generalized œdema of certain types of nephritis. In acute nephritis the greater portion of the salt taken in with the food is retained in the body and is not put out through the kidneys. Also, with the accumulation of ascites as a result of hepatic cirrhosis, or of œdema and transu-

dates following circulatory failure, the chloride excretion is decreased. On the other hand, chloride excretion is increased (up to 30 or even 60 gm.) during the resolution of pneumonia, or with the rapid absorption of exudates and transudates, or the absorption of œdema. This relation is to be explained by the fact that œdema fluid, as well as the exudate or transudate, shows a constant concentration of sodium chloride (approximately 0.65%).

For the **quantitative estimation of urinary chloride** by the method of Volhard-Arnold 10 c.c. of urine are mixed in a measuring cylinder of 100 c.c. capacity with 20 drops of pure (colorless) nitric acid and about 2 c.c. of ferric ammonium sulphate. Sufficient N/10 silver nitrate solution is then added from a burette to precipitate all the chloride as silver chloride. (When this point is reached the further addition of the silver solution results in no further precipitation; with normal urine 20 c.c. of the silver solution are sufficient.) The mixture is then diluted accurately to 100 c.c. with distilled water, shaken and filtered through a dry filter. It is now necessary to determine the excess of silver solution which has been added. To this end 50 c.c. of filtrate is titrated with N/10 ammonium thiocyanate solution until all the silver is precipitated as silver thiocyanate; when this point is reached the addition of a single drop in excess of the thiocyanate solution produces a wine-red color (ferric thiocyanate). The amount of thiocyanate solution required to produce this reaction in one half the filtrate, multiplied by two, and subtracted from the silver solution originally added, is equivalent to the number of c.c. N/10 silver solution required to precipitate, as silver chloride, the chlorides contained in 10 c.c. of urine. One c.c. of the silver solution is equivalent to 3.55 mg. chlorine or 5.85 mg. sodium chloride. From the resulting value the daily output of chloride may be calculated.

Sulphuric acid, H_2SO_4, daily output 2.0 to 2.5 gm., appears in the urine as preformed sulphuric acid bound to alkali or alkaline earths, or as ethereal sulphates combined with phenol, indoxyl and other substances, normally in the proportion of one part of the latter to 10 parts of the former. In carbolic acid poisoning almost the entire amount of sulphuric acid in the urine may be bound with phenol.

Phosphoric acid, H_3PO_4, daily output in the urine 2.5 to 3.5 gm. as a tribasic acid forms three varieties of salts: (1) the diacid = primary salts (e.g., NaH_2PO_4 = monosodium phosphates). These are soluble in water and give an acid reaction with litmus or phenolphthalein. (2) The monoacid = secondary salts (e.g. Na_2HPO_4) = disodium phosphates, which are also soluble in water, and are alkaline to litmus but not to phenolphthalein. A mixture of the monoacid and diacid phosphates, which reacts as neutral to litmus, is alkaline to lackmoid; the diacid phosphates must be present in considerable excess in such a mixture to produce an acid reaction to lackmoid. This fact is important in testing the urine with lackmoid solution in ether (Neubauer) as described on page 188. The mono-acid salts of the **alkaline**

FIG. 58.
Calcium carbonate, ball and biscuit forms.

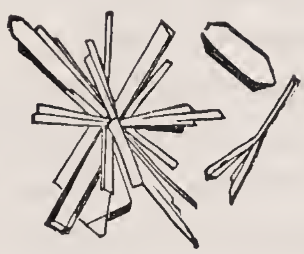


FIG. 59.
Calcium (monacid) phosphate.

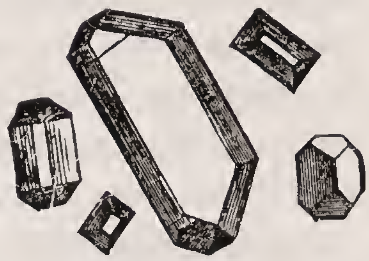


FIG. 60.
Ammonium-magnesium phosphate, coffin-lid crystals.

earths (calcium and magnesia), e.g., the mono-acid, (dibasic) calcium phosphate, $CaHPO_4$, are insoluble in water. (3) The tribasic-tertiary salts of alkalies (Na_3PO_4) = trisodium phosphate, are also soluble in water, are alkaline to litmus, lackmoid, and to phenolphthalein. The tricalcium and trimagnesium phosphates are insoluble in water, as is also ammonium-magnesium phosphate ($MgNH_4PO_4 + 6H_2O$), (Fig. 60) which appears in the urinary sediment in the form of coffin-shaped crystals. Phosphoric acid in the urine is bound in the proportion of 2/3 to alkali, to 1/3 to the alkaline earths. The daily output of earthy phosphates amounts to about 1.2 gm.

When the urine shows persistently an abundant sediment of calcium and magnesium phosphate and carbonate, the condition is known as **phosphaturia.** This finding represents an increase in the urinary output of calcium but is no evidence of an increased output of phosphoric acid. Phosphaturia may be caused by an overlarge intake of alkaline

waters or of alkaline carbonates or citrates. In many such cases the urine is cloudy or milky on voiding and clears with the addition of acetic acid.

Carbonates are present in the normal acid human urine only in small amounts, in somewhat larger amounts in neutral or alkaline urine, and particularly when the amount of alkali and alkaline earth is greater than may be bound by the other acids (hydrochloric, sulphuric, phosphoric, acetic, etc.). Carbonates are, therefore, increased upon a fruit or vegetable diet since such food contains large amounts of alkali and alkaline earths, and also with the administration of alkaline mineral water or of sodium bicarbonate. In the presence of large amounts of carbonates the urine foams on the addition of acids. Calcium carbonate appears in the sediment in the form of small balls or biscuits (Fig. 58) which dissolve upon the addition of acids.

Sodium, Na, daily output 4–6 gm.; **potassium**, K, 2–3 gm. In fever the amount of sodium falls while that of the potassium may be increased three to seven fold.

Ammonia, NH_3, appears uniformly (bound to acid) in unfermenting urine, but in only small amounts (0.3 to, at most, 1.0 gm.). It may increase to 2 or even 6 gm. a day when the quantity of the acid excreted in the urine is so great that the amount of alkali and alkaline earth are insufficient to neutralize it.

Urine undergoing decomposition may contain large quantities of ammonia and carbonate formed from decomposing urea so that a glass rod dipped in hydrochloric acid and held over the urine may produce a cloud of ammonium chloride.

Calcium, Ca, daily output on the average 0.16 gm.; **magnesium,** Mg, daily output about 0.23 gm. From 0.3 to 0.5 gm. Ca are excreted daily in the stools.

Calcium sulphate appears in the sediment in fine prisms and needles, which are insoluble in hydrochloric or acetic acid. **Mono-acid calcium phosphate** crystallizes in wedge-shaped crystals which gather into rosettes (Fig. 59); **ammonium-magnesium phosphate** (triple phosphate), in refractile coffin-shaped crystals. Both of the latter are easily soluble in acetic acid.

Iron appears in the urine in only very small amounts and

in organic combination. Its demonstration is, therefore, only possible in the ash of urine. The greater part of the iron, a large proportion of the calcium, and a variable amount of magnesium and phosphoric acid are eliminated through the intestines. The quantitative estimation of these substances in the urine can, therefore, give no accurate information concerning the total amounts excreted. For this purpose estimations must also be carried out upon the fæces.

Albumin

The protein molecule is unusually large and in solution exists only in the colloidal state. Upon its colloidal character depend the coagulability of a protein solution, and the effect of the addition of salts ("salting out"), and of alcohol, as well as the inability of the proteins in solution to dialyse through a membrane. By the action of the ferments of digestion, and of certain proteolytic enzymes present in tissue cells, the large protein molecules may be split into smaller components: polypeptides, albumoses and peptones. These compounds are not coagulable, but give the Biuret reaction, and are precipitated by phosphotungstic acid in the presence of sulphuric or hydrochloric acids. Albumoses may be precipitated by ammonium sulphate; peptones are not, but may be precipitated by potassium ferrocyanide and acetic acid. Upon further splitting by trypsin or strong acids the proteins produce a number of crystalloid substances, namely, amino-acids and diamino-acids. Among the amino-acids are: amino-acetic acid (glycocoll), aminopropionic acid (alanine), aminocapronic acid (leucine), aspartic acid (aminosuccinic acid), glutaminic acid, and the aromatic amino-acids, phenylalanine and tryosine, indolaminopropionic acid (tryptophane), and sulphur-containing cystine. The diamino-acids of the proteins are lysine, arginine, and histidine. Upon the fact that proteins contain these several constituents depends a series of color reactions: the Millon test (tyrosine); the dark color produced by heating with lead acetate and sodium hydroxide (cystine), and others. These constituents are so grouped that the basic NH_2-group of one amino-acid is always bound with the acid COOH-group of another. This linking of several amino-acids determines the Biuret reaction, which is characteristic of all proteins and also of

albumoses and peptone. Upon the optical activity of the amino-acids depends the lævo-rotation of protein, and upon the basic nature of the diamino-acids the fact that they are precipitated by certain reagents (phosphotungstic acid, picric acid, uranium acetate, potassium ferro-cyanide, and acetic acid). Some protein bodies, the so-called proteids, contain, in addition, certain other characteristic groups: phosphoric acid (casein), glucosamine (mucin), hæmatin (hæmoglobin), nucleic acid (nucleo proteid).

The protein of the blood serum, particularly serum albumin, appears in the urine with all forms of renal disease: in acute nephritis and in chronic nephritis with œdema in larger amounts, in arterio-sclerotic nephritis in small quantities or, at times, not at all. The absence of albumin from the urine is, however, no indication that the kidney is absolutely normal. Albuminuria also occurs with chronic passive congestion of the kidneys (with circulatory failure), with amyloid degeneration, with syphilis of the kidney, with certain types of poison which attack the kidney, with icterus, with many acute infections showing a high fever, in certain blood diseases, and finally, from time to time, in normal individuals after strenuous exercise. In some young individuals, otherwise healthy, albuminuria occurs when they stand upright and disappears upon rest in bed. This "orthostatic albuminuria" appears sometimes to be occasioned by disturbance of the circulation to the kidney caused by, or incident to, spinal lordosis. If the urine contain blood or pus, e.g., with disease of the bladder, it will, of course, contain albumin (albuminuria spuria) and in such cases it is necessary to determine whether the albumin content of the urine is approximately that of the amount of blood or pus present. If the albumin content is undoubtedly larger than can be accounted for by the amount of blood or pus present, a kidney lesion is to be suspected.

[The persistent excretion of albumin from the blood by the kidneys sometimes results in a conspicuous fall in the protein content of the serum. Normally about 7.0 gm.%, the serum protein may fall to 5.0 gm.% or less in cases of chronic nephritis or nephrosis. Such a reduction is accompanied by a fall in the osmotic pressure of the serum and

contributes to the development of œdema in these instances. Moreover, since protein excreted under these circumstances is principally derived from serum albumin the **albumin-globulin ratio** in the serum—normally 60/40 or above—may be inverted, i.e., the serum protein may be composed of 30% albumin and 70% globulin.]

Albumin may be demonstrated in the urine by the following tests: (turbid urine must be filtered before testing): I. **Heat and acid:** The urine is heated in a test tube to boiling and one or more drops of dilute acetic acid are then added (instead of dilute acetic, concentrated nitric acid may be used). If a precipitate develops during heating which disappears on addition of the acid, it is composed, not of albumin, but of the phosphates or carbonates of calcium or magnesium which are easily soluble in acid. If there remain even a slight clouding, or if such appear for the first time upon the addition of acid, albumin is present. If the urine is very dilute or poor in salt the addition of a small amount of salt greatly enhances the accuracy of the test.

From time to time a precipitate may appear in cold urine upon the addition of acetic acid, which consists of albumin (not of mucin). These protein bodies, precipitable by acetic acid, occur in icterus, orthostatic albuminuria and in many of the less severe forms of nephritis.

If the albumin precipitate is allowed to settle after boiling, and its volume measured after several hours it is possible to obtain an approximate estimate of the percentage albumin content of the urine. With an albumin content of 2–3%, the entire contents of the test tube are changed, upon heating, to a compact coagulum. With 1%, the albumin coagulum fills over half the column of urine; with 0.5%, one third; 0.25%, one fourth; 0.1%, one tenth; with 0.05%, only the cup at the bottom of the test tube is filled, and with smaller quantities than 0.01%, there appears only a cloudiness and no frank precipitate whatever. For a somewhat more exact estimation of the albumin content the **Esbach** albuminometer may be employed. This method is complicated by the fact that Esbach's reagent (picric acid and citric acid) may cause a precipitate, sometimes, in normal albumin-free urine, since the picric acid produces an insoluble compound with

the potassium salts, urates, quinine, urotropin and other substances. As a result the Esbach method may give too high a value following the use of urotropin, or may give a positive reaction in urines that contain no acids. [The use of Tsuchiya's reagent avoids this difficulty: 1.5 gm. phosphotungstic acid dissolved in a mixture of 5 c.c. concentrated HCl and 95 c.c. of 95% alcohol. Ed.]

Heller's test: Concentrated nitric acid is layered beneath the urine in a test tube by means of a pipette. In the presence of albumin there develops at the boundary between the two fluids a cloudy ring.

In very concentrated urines a precipitate may develop, which is due not to albumin but to uric acid (the ring stands higher, in the urine itself, and tends to spread), to urea nitrate (the precipitate is crystalline and only develops after standing) or to acids combined with resinous bases (after the administration of copaiba storax, turpentine, etc.; the precipitate dissolves in alcohol after cooling). The albumin ring may be colored blue or green in the presence of indigo or bile pigments.

Test with acetic acid and potassium ferrocyanide: A considerable amount of acetic acid and 3 to 5 drops of a 10% solution of potassium ferrocyanide are added to the urine without heating. In the presence of albumin or albumoses there develops a precipitate; with small quantities of albumin this precipitate appears only after several minutes.

Biuret test: The urine is alkalinized with potassium hydroxide and 1 to 3 drops of a very dilute copper sulphate solution are added. In the presence of albumin, albumose or peptone there develops a reddish-violet color.

Sulpho-salicylic acid test: If 20% sulpho-salicylic acid be added to the urine, there develops a definite clouding with small traces of albumin.

Albumoses appears in the urine in many febrile infectious diseases (febrile albumosuria), in some types of poisoning (e.g. phosphorus poisoning), also in the presence of a purulent exudate (empyema, meningitis [pyogenic albumosuria]), in pneumonia, in the puerperium, with ulcerative processes in the intestinal canal. The proof of the presence of albumoses is of very little diagnostic significance.

To test for albumoses it is necessary first to eliminate any albumin which may be present. Ten c.c. of urine are mixed in a test tube with 8 gm. of powdered ammonium sulphate and warmed to boiling. The precipitate is filtered off and, in order to remove the urobilin, is washed several times with alcohol. It is then taken up with a small amount of water, warmed to boiling and refiltered. The proteins which have been coagulated by the heating are not dissolved in the water; the albumoses, however, pass into solution. The Biuret test is then applied to this aqueous solution and if positive indicates the presence of albumoses.

With osteosarcoma and other diseases of the bone marrow (e.g., myeloma) there occurs a type of **protein** in the urine described by Bence-Jones. To demonstrate this protein the acid urine is warmed to about 60°. At this temperature a precipitate appears; this dissolves again on boiling to reappear as the mixture is again allowed to cool.

Blood

One speaks of **hæmaturia** when blood corpuscles are present in the urine, and of **hæmoglobinuria** when blood pigment is dissolved in the urine even though blood corpuscles are absent from the sediment. This latter condition occurs when the red blood corpuscles are broken down and their hæmoglobin is set free. Hæmoglobinuria occurs in many severe intoxications, i.e., with potassium chlorate, and with "paroxysmal hæmoglobinuria." In patients with this latter disease cooling or vigorous exercise may be sufficient to bring on an attack of fever and hæmoglobinuria. Regarding black water fever see page 305.

Hæmaturia occurs in acute glomerulonephritis or in an acute exacerbation of chronic nephritis. Hæmaturia also occurs with renal infarction, with parasites (distomiasis, filaria), with tumors and tuberculosis of the kidney and bladder, with stones in the pelvis of the kidney or bladder, with severe pyelitis and cystitis and with certain types of poisoning.

With **hæmorrhagic renal disease** the albumin content of the urine is increased out of proportion to the amount of blood present, and red-blood-cell casts appear in the sedi-

ment (Fig. 64). **Renal infarction** occurs with circulatory failure or bacterial endocarditis and is associated with transient hæmaturia, pain in the flank, and rise in temperature. With **renal calculus** hæmaturia occurs in paroxysms accompanied by severe renal colic. **Tumors of the kidney** (usually hypernephroma or carcinoma) or of the bladder give rise from time to time to profuse, and usually painless, bleeding. **Tuberculosis of the urogenital tract** is associated with persistent small amounts of blood in the urine; in this condition the tubercle bacilli are often demonstrable in the sediment. Hæmorrhagic **cystitis** is accompanied by pain in the bladder and dysuria; the urine is often purulent and partially decomposed, and sometimes contains bacteria. Transient hæmaturia, associated with dysuria, exaggerated with exercise, and decreasing with rest, is pathognomonic of **vesicle calculus.** It is important to remember that in women during **menstruation** the urine is usually mixed with blood. Following injury and with **disease of the urethra** there may be bleeding between voidings.

Urine containing blood pigment is either a bright red, has a greenish fluorescence due to the presence of hæmoglobin, or is dark brown or almost black (blackwater) due to methæmoglobin. The latter is differentiated from oxyhæmoglobin by spectroscopic examination. Methæmoglobin shows, in addition to the two oxyhæmoglobin bands in the yellow and green, an additional dark band in the red and a fainter band between the green and blue. There is usually some methæmoglobin in any urine containing hæmoglobin. **Hæmatin** is sometimes present in the urine and shows, under the spectroscope, a band in the red very smilar to that of methæmoglobin but with the difference that upon the addition of ammonium sulphate and ammonia there appears the band in the green characteristic of reduced hæmatin, and another band somewhat to the right, while the reduction of methæmoglobin with ammonium sulphate brings out the characteristic bands of reduced hæmoglobin (see page 134).

In addition to spectroscopic examination the following tests serve to demonstrate blood pigment in the urine:

Heller's test: The urine is made strongly alkaline with potassium hydroxide. The alkaline phosphates are thus

thrown out of solution and carry down with them the blood pigment. Upon standing they appear reddish-brown in the presence of blood pigment whereas they are normally white.

Van Deen's test: (Guaiac test): This test depends on the ability of the blood pigment and its iron-containing derivatives to act as peroxidases, e.g., to accomplish the transfer of oxygen from a peroxide to an easily oxidizable substance. The urine is mixed with 1/10 its volume of glacial acetic and above it is layered a mixture of equal parts of fresh tincture of guaiac and hydrogen peroxide (or old oil of turpentine); in the presence of blood a blue ring develops at the interface. Since this test may be positive in urine which contains pus but no blood it is obviously applicable only in the absence of pus. This error may be avoided if the urine is either previously heated or treated with 1/6 its volume of concentrated acetic acid, shaken with a few c.c. of ether[1] and the ether extract used for the guaiac test. In the presence of blood pigment the ether is colored a reddish-brown by the acid hæmatin and when treated with tincture of guaiac and turpentine becomes blue. If the test is obviously positive the hæmatin contained in the ether may be reduced and demonstrated with a spectroscope.

Somewhat more sensitive than the Guaiac test is the **Benzidine test:** To an acid ethereal extract of urine is added a small amount of a saturated alcoholic solution of benzidine and a few drops of 3% hydrogen peroxide. In the presence of blood a greenish-blue color appears.

Very small amounts of blood, too small to be recognized by any of these tests, may still be demonstrated by microscopic examination of the urinary sediment for red blood cells.

Porphyrinuria: In severe cases of poisoning with sulfonal, trional, or veronal, as well as with certain acute diseases accompanied by vomiting, pain in the legs and constipation, the urine is dark red in color due to the presence of porphyrin. This may be demonstrated by spectroscopic examination of a thick layer. Certain rare cases excrete persistently

[1]Old ether contains substances which interfere with the reaction. These may be removed if the ether is repeatedly shaken with ¼ its volume of 15% potassium hydroxide and allowed to stand overnight.

burgundy-red urine containing porphyrin. These cases of so-called chronic or congenital porphyrinuria show blister-like bullæ over those portions of the skin exposed to the light which lead, in the end, to wide-spread scar formation, and when they occur over the eyes, to complete blindness. The red pigment in such urine is urinoporphyrin, described by H. Fischer ($C_{44}H_{36}N_4O_{16}$), and is demonstrable in small quantities also in the fæces of such patients. These substances appear to be related to, but not identical with, hæmatoporphyrin ($C_{34}H_{33}N_4O_6$), which is formed from hæmatin by the withdrawal of iron under the action of acids. The porphyrins are apparently derivatives of a hæmoglobin-like pigment contained in the tissues (myohæmoglobin). To test for urinoporphyrin glacial acetic acid is added to the urine, drop by drop, until a red precipitate appears. This is allowed to settle, filtered, taken up with acid alcohol and examined spectroscopically. Or to a large quantity of urine may be added 1/5 its volume of 10% sodium hydroxide. The phosphates are thus precipitated and carry down the pigment. This precipitate is washed with water, then with alcohol, and then dissolved on the filter by the addition of about 2 c.c. of acid alcohol. The filtrate upon spectroscopic examination shows a band in the yellow and green (see table of spectra, page 134). If, now, ammonia is added and the mixture refiltered, four bands appear in the red, yellow, green, and blue. Upon the addition of an ammoniacal solution of zinc chloride two bands appear similar to those of oxyhæmoglobin.

Bile pigments: [Under certain conditions, i.e., with obstruction of the bile ducts or widespread necrosis of the liver cells, bilirubin is regurgitated into the blood together with bile salts. The presence of the surface-active bile salts prevents the adsorption of bilirubin to the protein, and allows its excretion by the kidneys and its appearance in the urine. With other types of jaundice, i.e., those resulting from overproduction of bilirubin and/or subnormal hepatic function, e.g., hæmolytic icterus or lobar pneumonia, the bilirubin is adsorbed by the serum proteins and its excretion by the kidneys is thus prevented. The first type is associated with clinical jaundice and bilirubinuria; in the second type

although skin and scleræ may be jaundiced bile may not be demonstrable in the urine. Urine containing bilirubin is brown in color and upon shaking produces a yellow foam. Upon extraction with chloroform the bilirubin discolors the chloroform with a golden-yellow tint. Ed.]

Bilirubin is identified by the **Gmelin test.** Below the urine in a test tube is layered a small amount of fuming nitric acid. At the interface between the two solutions, in the presence of bilirubin, there is formed a ring of color which changes from green through violet to red and finally yellow. A blue ring may be caused by the presence of indigo, and reddish-brown ring by urobilin and other substances. The Gmelin test may be carried out in another fashion. If the urine is filtered the greater part of the bile pigments remain upon the filter paper. If upon this yellowish filter paper is placed a small drop of nitric acid the characteristic rings of color form about it. Or several drops of urine may be placed upon an unglazed porcelain plate and touched with a rod dipped in nitric acid.

Huppert's test is more exact. The urine is mixed with barium hydroxide, the resultant precipitate is filtered off and heated with alcohol to which several drops of dilute sulphuric acid have been added. In the presence of bilirubin the alcohol takes on a green color.

If bile-containing urine is mixed with Lugol's solution a greenish color appears. The same test may be carried out by carefully layering tincture of iodine, diluted ten times, above the urine in the test tube. At the surface of contact there appears a grass-green ring.

The **method of Ehrlich and Proescher** consists in saturating 10 c.c. of urine with about 8 gm. of ammonium sulphate, filtering the colored precipitate on a fine folded paper filter, and extracting with alcohol. To the alcoholic extract are then added hydrochloric acid and Ehrlich's diazo solution (page 222). In the presence of bilirubin the solution becomes a beautiful blue and, upon the addition of potassium hydroxide, there forms a ring of color, green, red and blue.

Minute traces of bile pigment which are not demonstrable with these tests may sometimes be recognized upon microscopic examination of the urinary sediment in that the casts,

epithelial cells and leucocytes appear discolored and yellowish.

Urobilin: By the action of the intestinal bacteria bilirubin is transformed to urobilinogen. This is in part excreted in the stools and in part resorbed through the intestinal wall and borne to the liver by the portal circulation. Here it is largely absorbed and is probably utilized in the formation of bilirubin or hæmatin. Under normal conditions only a small amount of urobilinogen appears in the urine where it is rapidly oxidized to urobilin. With subnormal hepatic function, or if bilirubin be formed in excessive amounts, relatively less urobilinogen is removed by the liver and urobilin may be demonstrably increased in the urine. (See page 143.) [Ed.] This occurs with various types of liver disease and in particular with hepatic cirrhosis, chronic passive congestion of the liver, with cholelithiasis, with certain types of jaundice, with pernicious anæmia, and also during the absorption of hæmorrhage (hæmorrhagic infarction, apoplexy, etc.). With complete occlusion of the ductus choledochus neither urobilin nor urobilinogen appears in the urine.

Urobilin is demonstrated in the urine as follows: The urine is mixed with an equal volume of **Schlesinger's reagent** (zinc acetate 10 gm., alcohol 100 c.c.). The turbid mixture is then shaken and filtered. In the presence of urobilin the filtrate shows a green fluorescence (best seen by looking down the test tube against a dark background). This test may be rendered more sensitive by mixing 3 drops of a 5% alcoholic solution of iodine with 10 c.c. urine to convert all the urobilinogen to urobilin before the addition of the Schlesinger's reagent. Upon spectroscopic examination urobilin-containing urine shows a single absorption band between the green and blue (sometimes only after the addition of zinc chloride and ammonia).

Urobilinogen is the precursor of urobilin; the latter is formed from urobilinogen only after the urine has stood for some time. It is, therefore, advisable to test for urobilinogen only in a freshly voided specimen. To test for **urobilinogen** (**Neubauer's test**) add to the urine a few drops of a 2% solution of dimethylparaminobenzaldehyde in 5% hydrochloric

acid. In the presence of large quantities of urobilinogen a red color appears in the urine in the cold but in normal urine only after heating. If this color fails to appear even after boiling it may be assumed that the urine contains no urobilinogen (with occlusion of the common bile duct, with diarrhœa). A similar reaction is given by the indol-forming groups of the proteins but only in the presence of concentrated hydrochloric or sulphuric acid. Since indol is usually present in the stool, the aldehyde reaction in the extract of stool may not be regarded as conclusive proof of the presence of derivatives of the bile pigment.

Melanin. In the urine of patients with melanotic sarcoma there may appear melanogen which, upon treatment of the urine with ferric chloride or chromic acid, produces a black cloud of melanin. In some cases the urine may be black with previously formed melanin. Urine containing melanin gives a positive **Thormahlen test:** Upon performing the Legal's acetone test with sodium nitroprusside and potassium hydroxide, upon the addition of concentrated acetic acid there appears in melanogen-containing urine a beautiful blue color.

Sugar. Among the carbohydrates the following groups are to be distinguished (to mention only the medically important members of each):

Monosaccharides, $C_6H_{12}O_6$.

Grape sugar-glucose, dextro-rotatory, reduces, ferments.

Fructose-lævulose, lævo-rotatory, reduces, ferments.

Galactose, dextro-rotatory, reduces, does not ferment with pure yeast.

Disaccharides, $(C_{12}H_{22}O_{11})$.

Cane sugar, dextro-rotatory, does not reduce, does not ferment directly with pure yeast, splits under the action of acids into dextrose and lævulose, which reduce and ferment.

Lactose, dextro-rotatory, reduces, does not ferment, forms, upon splitting, dextrose and galactose.

Maltose, dextro-rotatory, reduces, ferments, and splits into two molecules of dextrose.

Polysaccharides, $(C_6H_{10}O_5)_n$.

Starch, swells in water; fails to ferment or to reduce, and

is transformed by digestion into dextrin, maltose and grape sugar.

Dextrin and glycogen, produce in water a cloudy solution, fail to ferment or to reduce and are split into several molecules of grape sugar.

Grape-sugar (glucose) is present in the normal urine only for a short time after the ingestion of large amounts of sugar. If, following the administration of 100 gm. of sugar or less by mouth, glycosuria appears, one speaks of alimentary glycosuria, e.g. with hyperthyroidism or following the administration of thyroid extract, with certain types of neurosis, with excessive indulgence in beer, and with certain types of obesity and arteriosclerosis. If glycosuria persists one is usually dealing with a case of diabetes mellitus. Transient glycosuria may also occur with certain poisons, e.g. carbon-monoxide, with meningitis, with cerebral hæmorrhage, with syphilis and certain other diseases of the nervous system, and finally with tumors of the hypophysis or adrenals.

Glucose may be recognized by the following characteristics:

1. through the action of yeast it is fermented, producing alcohol and carbon-dioxide;

2. upon boiling with potassium hydroxide it gives a brown color;

3. in alkaline solution it reduces metallic hydroxides, e.g. copper or bismuth oxide;

4. it rotates a beam of polarized light to the right;

5. with phenylhydrazine it produces crystalline glucosazone.

Fermentation test carried out as follows: To the urine is added a little fresh yeast, and a fermentation tube is filled with the mixture until no air bubbles remain in the vertical portion of the tube. The tube is then allowed to stand in a warm place. In the presence of glucose, after several hours, carbon-dioxide collects at the top of the tube. In order to demonstrate that the gas which has collected is really carbon-dioxide, and not perhaps a bubble of air, a little potassium hydroxide may be added to the tube with the result that carbon-dioxide is rapidly absorbed. In order to be absolutely certain of the result this test may be controlled by a mixture

of a glucose solution and yeast, on the one hand, and of water and yeast on the other. By means of the first it is possible to ascertain that the yeast is active, and by the negative result of the third test that it is sugar-free. The fermentation test is the most certain of all the sugar reactions and should always be applied when any of the other reactions give doubtful results. The apparatus devised by Lohnstein is extremely useful in that the amount of carbon-dioxide formed may be measured and the sugar content calculated therefrom.

Moore's test. The urine is mixed with 1/3 its volume of concentrated potassium hydroxide and boiled for several minutes. In the presence of sugar a brown color appears. This test is only to be regarded as positive when the resulting color is intense.

Reduction Tests:

Tromer's test. Add to the urine 1/3 its volume of potassium or sodium hydroxide and 1 to 3 drops of a dilute (5%) solution of copper sulphate. If the cupric hydroxide, which is formed, and which has a bright blue color remains as a flocculent precipitate even after shaking, no sugar is present. In the presence of sugar, glycerin, tartaric acid or ammonia, the cupric hydroxide goes into solution producing a blue color, or in the presence of protein a violet tint. The copper sulphate should then be added drop by drop until a small amount remains undissolved after shaking. Upon warming this mixture, if sugar be present, at the boiling point or slightly below there forms a red precipitate of cuprous oxide or a golden-yellow precipitate of cuprous hydroxide due to the action of the sugar in withdrawing oxygen from the cupric oxide. If the solution becomes decolorized, or the precipitate fails to appear or does so only after cooling, the test must be regarded as uncertain since other reducing substances may be present in the urine (e.g. uric acid or creatinine) which cause the cuprous oxide to remain in solution. In addition certain reducing bodies, e.g. glycuronic acid, may appear in the urine following the administration of various drugs (turpentine, chloral hydrate, chloroform, benzoic acid, salicylic acid, camphor, copaiba). Such substances, however, bring about

only a minimal amount of reduction. In alkaptonuria the urine also possesses reducing properties (see page 223).

Fehling's test. For this test two component solutions are prepared: (a) 34.64 gm. crystalline copper sulphate dissolved in water and diluted to 500 c.c.; (b) 173 gm. of Rochelle salt (potassium-sodium tartrate) and 100 c.c. of pure sodium hydroxide diluted to 500 c.c. with water. These two solutions are mixed in equal proportions before using. One c.c. of the mixture should be completely reduced by 0.005 gm. of glucose. Two c.c. of this solution are placed in a test tube, diluted with an equal volume of water and boiled. In the absence of contamination no evidence of reduction should appear. One or 2 c.c. of urine are added to the tube and the mixture heated on a water bath. In the presence of glucose there appears a reddish-yellow precipitate of cuprous oxide.

The quantitative determination of the urinary sugar by Fehling's method is carried out as follows: Ten c.c. of Fehling's solution, 10 c.c. of concentrated sodium hydroxide and about 50 c.c. of water are mixed in a dish. The urine is then added gradually from a burette until the blue color of cupric oxide has completely disappeared. The percentage content of sugar is then calculated from the fact that the volume of urine added must have contained .05 gm. of glucose. If the sugar content is known to be high it is sometimes better to dilute the urine 1 to 10.

Benedict's methods. Qualitative method: A delicate test, and less liable than others to give a falsely positive result. Benedict's **qualitative reagent** is prepared as follows: Dissolve (with heat if necessary) 173 gm. sodium citrate and 100 gm. anhydrous (or 200 gm. crystallized) sodium carbonate, in 700 c.c. water. Add slowly 17.3 gm. copper sulphate dissolved in 100 c.c. water. Cool and dilute to 1000 c.c. with distilled water.

Method: To about 5 c.c. of the reagent in a test tube add 8–10 drops (no more) of urine, boil the mixture for 2 minutes and allow to cool. Dependent upon the amount of glucose present the reagent turns green, or a green, yellow or red precipitate appears; the first may occur with urine having a "high normal" content of glucose, the last indicates the presence of 1% glucose or more.

Benedict's **quantitative reagent** contains potassium thiocyanate as well as copper sulphate. In the presence of the former a white precipitate of cuprous thiocyanate is formed on reduction instead of the usual red precipitate of cuprous oxide. Potassium ferrocyanide is added to aid in keeping cuprous oxide in solution. The precipitate formed is white so that the loss of all blue tint in the solution, indicating complete reduction of the copper, is readily observed.

Reagent: 18.0 gm. copper sulphate (crystallized), 200 gm. crystallized sodium carbonate (one-half the weight of the anhydrous salt may be used), 200 gm. sodium or potassium citrate, 125 gm. potassium thiocyanate, 5 c.c. potassium ferrocyanide (5% solution), distilled water until total c.c. = 1000.

Method: The urine is poured into a 50 c.c. burette up to the zero mark. Twenty-five c.c. of the reagent are measured with a pipette into a porcelain evaporation dish (25-30 cm. in diameter), 10–20 gm. of crystallized sodium carbonate (or one-half the weight of the anhydrous salt) are added, together with a small quantity of powdered pumice stone or talcum, and the mixture heated to boiling over a free flame until the carbonate has entirely dissolved. The diluted urine is now run in from the burette, rather rapidly, until a chalk-white precipitate forms and the blue color of the mixture begins to lessen perceptibly, after which the solution from the burette must be run in a few drops at a time, until the disappearance of the last trace of blue color, which marks the end point. The solution must be kept vigorously boiling throughout the entire titration.

Calculation: The 25 c.c. of copper solution are reduced by exactly 50 mg. of glucose. Therefore the volume run out of the burette to effect the reduction contained 50 mg. of the sugar. When the urine is diluted 1 : 10, as in the usual titration of diabetic urines, the formula for calculating the per cent of the sugar is as follows: $\frac{0.050}{X} \times 1000 = \%$ in original sample, wherein X is the number of cubic centimeters of the diluted urine required to reduce 25 c.c. of the copper solution.

Bœttger's test. The urine is made alkaline by the addition of sodium hydroxide, or by saturation with sodium carbonate;

a small amount of crystalline bismuth subnitrate is added, and the mixture boiled for several minutes. Or the urine may be boiled with one-tenth of its volume of Nylander's solution (Rochelle salt 4.0 gm., 10% sodium hydroxide 100 c.c.; 2 gm. bismuth subnitrate are added while the mixture is warmed; the solution must then be filtered). In the presence of glucose there appears a dark brown color due to the separation of metallic bismuth. The test is not applicable to albuminous urine and gives sometimes confusing results.

Polarization. The specific rotation by glucose of the yellow light of a sodium arc α (D) amounts to 52.8°. From the amount of rotation produced by a given specimen, and the length of the tube expressed in decimeters, may be calculated the percentage content of glucose (P) in the urine by the formula $P \times \frac{\alpha . 100}{52.8' \times 1}$. It is most convenient to use a polarimeter tube 1.893 dm. in length which makes it possible to read directly from the scale the sugar content in per cent. Certain polarimeters are equipped with a scale graduated in percentage glucose instead of in degrees and minutes. Since, in the presence of lævo-rotatory substances, e.g. albumin or β-oxybutyric acid, polarization determinations give too low results it is advisable, in such cases, to ferment the urine before attempting polarimetry. In case lævo-rotation is present after fermentation this value must be added to that of the dextro-rotation observed in the unfermented specimen. If the urine be dark colored or cloudy it is impossible to examine it directly with a polarimeter. It is then necessary to decolorize and clear by adding a small amount of lead acetate or animal charcoal, shaking and filtering. The filtrate is then examined in the polarimeter. Polarimetry is perhaps the most simple method of determination of sugar and gives, particularly with the modifications outlined above, very exact results.

Phenylhydrazine test. A few grains of phenylhydrazine hydrochloride and a slightly larger amount of sodium acetate are dissolved in a few c.c. of water and warmed. To this is added an equal volume of urine and the mixture is heated upon a water bath for twenty minutes and then allowed to cool. In the presence of considerable quantities of glucose

there forms, after a few minutes, a precipitate composed of yellow clusters of needle-like crystals of phenylglucosazone.

Lævulose may only be demonstrated in the urine when no glucose is present. The urine then is lævo-rotatory; but otherwise gives all the tests for sugar, i.e. reduces, ferments with yeast and forms phenylglucosazone. When dextrose and lævulose are present simultaneously the lævo-rotation of lævulose is obscured by the dextro-rotation of dextrose. In this event the titration with Fehling's solution gives higher results than the findings on the polarimeter would indicate, due to the fact that, whereas in the polarimeter the dextro-rotation of dextrose is reduced by the lævo-rotation of lævulose, in reduction tests, the reducing power of lævulose, being the same as that of dextrose, is added to it. Lævulose-containing urine gives a positive reaction to Seliwanoff's test: The urine is warmed with several crystals of resorcine and half its volume of concentrated hydrochloric acid; in the presence of lævulose there appears a red color and a dark precipitate which redissolves upon the addition of alcohol.

Lactose ($C_{12}H_{22}O_{11}$) is sometimes found in the urine of pregnant women and in the early stages of lactation, particularly if the breasts be overfilled with milk. It is dextrorotatory, does not ferment with yeast but does so with lactic acid, reduces cupric oxide, and forms with phenylhydrazine yellow crystals of phenyl-lactosazone.

In certain cases there may appear in the urine a **pentose,** i.e. a form of sugar with 5 carbon atoms, e.g. arabinose ($C_5H_{10}O_5$). Such urine forms a red color upon boiling with phloroglucine or orcine and concentrated hydrochloric acid. This urinary pentose (arabinose) is optically inactive, reduces copper, fails to ferment with yeast, and yields with phenylhydrazine a pentosazone. Pentosuria is without diagnostic significance; it is observed, sometimes, in several members of a family.

Closely related to the sugars is glycuronic acid, CHO.-$(CHOH)_4$.COOH. This is never present free in the urine but always combines with phenols or indoxyl, or after the administration of camphor as camphoglycuronic acid. These glycuronic compounds are lævo-rotatory while the free acid is dextro-rotatory. A specimen of urine containing conjugated

glycuronic acid reduces copper, fails to ferment yeast, and rotates a beam of polarized light to the left, a phenomenon which disappears following heating with strong sulphuric acid or gives way to dextro-rotation on account of the formation of free glycuronic acid. Upon heating with orcinol and HCl the urine assumes a green color.

Acetone, diacetic acid and oxybutyric acid are closely related as their formulæ indicate:

$$\begin{array}{ccccc}
\gamma CH_3 & CH_3 & CH_3 & CH_3 & CH_3 \\
| & | & | & | & | \\
\beta CH_2 & CHOH & C=O & C=O & CH \\
| & | & | & | & \| \\
\alpha CH_2 & CH_2 & CH_2 & CH_3 & CH \\
| & | & | & & | \\
COOH & COOH & COOH & & COOH \\
\text{Butyric} & \beta\text{-Oxybutyric} & \text{Diacetic} & \text{Acetone} & \text{Crotonic} \\
\text{Acid} & \text{Acid} & \text{Acid} & & \text{Acid}
\end{array}$$

Diacetic acid is present in the urine during fasting or during the administration of a diet containing no carbohydrate; in addition it may appear in certain febrile diseases (particularly in children), rarely with advanced tuberculosis or with certain forms of enteritis. It is present in large amounts in severe cases of diabetes mellitus with impending coma.

Acetone occurs in any specimen of urine which contains diacetic acid. It is formed from diacetic acid. Every specimen of urine which contains diacetic acid gives, therefore, a positive reaction for acetone. In the various conditions mentioned above acetone may be detected not only in the urine but also by a fruity odor in the expired air, (Lieben's test) (see below).

β-oxybutyric acid is constantly found in specimens of urine containing acetone and diacetic acid. It occurs after fasting over long periods, sometimes with severe infectious diseases, and particularly in severe cases of diabetes mellitus.

If large quantities of diacetic and β-oxybutyric acids be demonstrable in the urine in cases of diabetes mellitus it is to be assumed that abnormal amounts of acid are present in the organism and should serve as a warning of impending acidosis and diabetic coma. In such cases it is necessary to exercise caution in prescribing a diet. Under these circum-

stances it is advisable to prescribe a strict diabetic regime. These "acetone bodies" may best be eliminated by the intelligent administration of insulin. In non-diabetic conditions they may be caused to disappear almost at once by the administration of carbohydrate.

To **test for acetone** the urine is treated with several drops of a freshly prepared solution of sodium nitroprusside and rendered strongly alkaline by the addition of concentrated sodium hydroxide. In any specimen of urine a red color appears following this procedure due to the presence of creatinine. If, however, several c.c. of concentrated acetic acid be added this red color disappears from the normal urine while in the presence of acetone or diacetic acid there develops a purplish-red or wine color (**Legal's test**). A similar color appears in the urine also following the administration of certain drugs, e.g., aloes or phenolphthalein. In the presence of melanin a blue color appears. It is sometimes better to treat from 1–500 c.c. of urine with a few drops of hydrochloric acid, to distill the mixture in a Liebig condenser and to test the distillate for acetone by means of **Lieben's reaction:** The addition to several c.c. of the distillate of several drops of Lugol's solution causes, in the presence of acetone and diacetic acid, the formation of a yellowish-white precipitate of iodoform.

In the presence of **diacetic acid** the urine gives a positive reaction to **Gerhardt's ferric chloride test:** The urine is mixed in a test tube with several drops of a solution of ferric chloride. This causes the formation (even in normal urine) of a greyish-white precipitate of phosphate of iron. If diacetic acid be present there appears, in addition to this precipitate, a burgundy-red color. Any specimen of urine which contains diacetic acid will always give a positive test for acetone. The reddish-brown color of the urine is not produced by diacetic acid alone but also by antipyrin and certain other drugs, as well as by amino-acids, with this difference, however, that the diacetic acid-containing urine also gives a positive test for acetone. Salicylic acid produces a violet color with ferric chloride.

β-oxybutyric acid rotates a beam of polarized light to the left ($D = -24.1°$) and breaks down on heating with sulphuric acid.

In the presence of large amounts of β-oxybutyric acid the

urine may become lævo-rotatory after fermentation and clearing with lead acetate and ammonia. For the quantitative estimation about 200 c.c. of urine are saturated with ammonium sulphate and made strongly acid with sulphuric acid. The oxybutyric acid is then extracted in an extraction apparatus or by repeated shaking with ether. The ether is evaporated off and the residue taken up with 20 c.c. of water, filtered, and examined in the polarimeter. From the degree of lævo-rotation the percentage content of oxybutyric acid may be calculated from the formula outlined on page 218. One degree rotation in a 2 decimeter tube corresponds to an oxybutyric acid content of 2.073%. On account of the close relationship of acetone, diacetic acid and oxybutyric acid the **quantitative determination** is best undertaken by the method

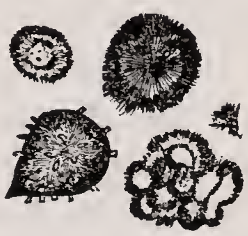


FIG. 61.—Leucine.

FIG. 62.—Tyrosin.

of **Van Slyke** (J. Biol. Chem. 1917, 32) in which the oxybutyric and diacetic acids are oxidized by means of potassium bichromate to acetone and all the acetone bodies determined together.

Diazo reaction (Ehrlich). Diazobenzol-sulphuric acid unites with certain unknown but presumably aromatic substances in the urine to produce a color.

The reagent is made up of two solutions: (a) Sulfanilic acid, 5.0, hydrochloric acid 50.0, distilled water 1000. (b) Sodium nitrite 0.5, water 100. These are mixed just before using in the proportion of 25 c.c. of solution (a) and 10 drops of solution (b). Equal parts of the reagent and the urine are mixed in a test tube with 1/8 volume of ammonia and the mixture shaken. In certain febrile diseases there appears a reddish color in the fluid (scarlet, carmen or vermilion) which is particularly striking in the foam. This is an almost constant finding in the urine after the first week of typhoid fever; here it is of diagnostic significance. It is also met with

in typhus fever, certain cases of pneumonia, puerperal fever and measles (seldom with scarlatina). The diazo-reaction may also be positive with tuberculosis and Hodgkin's disease and is taken by some to indicate a grave prognosis. A strongly positive diazo-reaction is met with in cases of trichinosis at the time of the development of the trichinæ.

Hydrogen sulphide is formed in the urine by the action of certain bacteria, i.e., with bacilluria and cystitis. Inasmuch as it is formed in normal urine on standing it is advisable to test for it only in a freshly voided specimen. About 50 c.c. of urine are placed in a flask with a two-hole stopper through which one tube passes down beneath the solution and the second forms an outlet. If, now, air is passed through the first tube and the piece of filter paper moistened with lead acetate solution is held in front of the outlet there appears on the paper after a few minutes a brownish discoloration due to lead sulphide.

Amino acids. Leucine and tyrosine are found in the urine in some cases of acute yellow atrophy of the liver, phosphorous poisoning and, more rarely, in certain other severe diseases. Leucine is present in yellowish refractile balls which often appear to have radial striations, tyrosine in sharp bundles or clusters of needles. To demonstrate these substances the urinary sediment is examined microscopically. It is best to treat the urine with basic lead acetate, to filter and then to remove the lead from the filtrate by bubbling hydrogen sulphide through it. The filtrate is then evaporated to a small volume and examined for crystals after standing. Leucine and tyrosine are easily dissolved in ammonia and may be recrystallized from a hot ammoniacal alcoholic solution.

Cystine is present in the urine with a peculiar, and sometimes hereditary, anomaly of metabolism known as cystinuria. Cystine appears in the sediment in shining, regular hexagonal plates which are easily soluble in ammonia. Small amounts may be demonstrated by microscopic examination of the precipitate formed when the urine is treated with acetic acid. Cystine may sometimes be recognized in urinary calculi.

Alkaptonuria. In this condition the urine, which is pale

upon voiding, becomes dark brown upon exposure to the air or upon shaking with potassium hydroxide. Upon the addition of a drop of dilute ferric chloride solution such urine gives a transient blue color. It reduces Fehling's solution but exhibits none of the other characteristics of urine containing sugar (optical activity, fermentation). Alkaptonuria often occurs in families and may persist for some time but is without pathological significance.

Lipuria. The urine is sometimes cloudy with fat (chyluria). This clouding disappears if the urine be treated with potassium hydroxide and shaken with ether. Ether dissolves the fat and, upon evaporation, leaves a fatty residue. Lipuria occurs if a communication be somehow established between the larger lymphatic channels and the urinary tract (occasionally with filariasis sanguinis), and with diseases involving the thoracic duct.

Tests for Drugs

Iodine and bromine. The urine is mixed with fresh chlorine water or strong, fuming nitric acid and extracted with several c.c. of chloroform; in the presence of iodine the chloroform is colored a bright red, and of bromine a yellowish-brown. The following test for iodine is rather more sensitive: The urine is made acid with hydrochloric acid, several drops of dilute starch paste are added, and, drop by drop, a solution of calcium chloride. Iodine causes the appearance of a bluish color.

Lead. Two liters of urine are evaporated in a porcelain dish to one fifth the volume, and mixed with an equal quantity of concentrated hydrochloric acid. While the mixture is still warm potassium chlorate is added, a small amount at a time, until decolorization is complete. Evaporation is continued until the odor of chlorine entirely disappears. The excess acid is now neutralized and, after filtration, hydrogen sulphide is passed through the filtrate: brown color produced by lead sulphide.

Arsenic. After destruction of the organic substances by hydrochloric acid and potassium chlorate (see above) the fluid is examined in Marsh's apparatus in which hydrogen is

produced by the action of hydrochloric acid upon arsenic-free zinc. The arseniuretted hydrogen then forms a film.

Mercury. To a 24-hour specimen of urine are added 10 c.c. of hydrochloric acid and either a small piece of pure copper wire or a leaf of gold foil; the mixture is then warmed. After 24 hours the urine is poured off, the metal is washed several times with water to which a trace of potassium hydroxide has been added, rinsed with alcohol and ether, and allowed to dry in the air. The metal is then placed in a long, carefully dried test tube and the end of the tube is heated red-hot. The mercury, which has formed an amalgam with the metal, is vaporized by this procedure and condenses upon the cool portion of the tube; upon exposure to iodine gas it may then be changed to mercuric iodide, which is red in color, and which, by careful warming, may be collected as a sharp ring upon the wall of the test tube. Concerning the demonstration of minute quantities of mercury by precipitation with iron see **Munch. Med. Wchnschr. 1915, p. 1183.**

After the administration of **chloral hydrate** the urine reduces Fehling's solution, gives a positive reaction with Moore's test for sugar, but does not, however, ferment with yeast. It rotates a beam of polarized light to the left on account of the presence of a compound of chloral and glycuronic acid. Certain other drugs, e.g. camphor and some of the phenols appear in the urine linked with glycuronic acid and cause lævo-rotation (see page 219).

Carbolic acid (phenol C_6H_5OH). Following the ingestion of considerable quantities of carbolic acid or lysol the urine assumes a greenish-brown color which deepens upon standing in the air; the same is true of the urine following the administration of hydroquinone ($C_6H_4(OH)_2$), Fol. uvæ ursi and tar. All drugs, which contain a phenol nucleus, may produce this dark color in the urine. With regard to the relation of the sulphates to phenol poisoning as well as the demonstration of carbolic acid see pages 197 and 200.

Salicylic acid (oxybenzoic acid). The urine produces a violet color with ferric chloride. The same is true following the administration of salol and other salicylates.

Antipyrine. Red color with ferric chloride.

Pyramidon. Upon layering tincture of iodine above the urine there develops, at the interface, a violet ring.

Turpentine. The urine smells of violets and sometimes gives a precipitate with nitric acid.

Tannin is excreted in the urine as gallic acid; the urine becomes dark blue upon the addition of ferric chloride.

Santonin. The urine is straw-colored, becomes scarlet upon the addition of alkali and, with Fehling's solution, turns first dark green and then a deep violet, after the addition of acetic acid green.

Rheum and senna (chrysophenic acid). The urine becomes red immediately following the addition of alkali and this color persists (in contrast to that caused by santonin). Upon the addition of barium hydroxide, with rheum and senna the **precipitate** is red, with **santonin** the **filtrate.** After extraction of the urine with ether, if it contain rheum or senna the color is demonstrable in the ether; with santonin the color does not go over into the ether.

Balsamum copaivæ and **oleum santali.** The urine gives a red color upon warming with hydrochloric acid.

Phenolphthalein sometimes used as a laxative. The urine turns bright red upon the addition of alkali.

URINARY SEDIMENT

The normal urine is clear upon voiding and, after standing, there settles out only a faint cloud, in which are to be found upon microscopic examination, a few leucocytes, epithelial cells and strands of mucus. If a genuine sediment be present it may consist either of so-called formed elements, e.g., leucocytes, red blood corpuscles, epithelial cells from the bladder or upper urinary passages, or renal casts, or of chemical substances which were dissolved in the urine and which have precipitated upon standing and cooling. In the first case the sediment is coarse and incompact. In the latter the sediment is compact, and that which is formed in an acid and concentrated urine is usually brick-red (acid urates). Free uric acid in whetstone-shaped crystals may settle out from a strongly acid urine. The sediment in an alkaline or neutral urine is usually white and consists in the main of alkaline phosphates or carbonates of calcium and magnesium. In urine which has

undergone ammoniacal decomposition there appears, in addition to these latter substances, ammonium-magnesium-phosphate and ammonium urate.

It is advisable to examine microscopically the sediment obtained by centrifugation of a freshly voided specimen of urine. If no centrifuge is available the urine may be allowed to stand in a pointed glass and the sediment withdrawn with a pipette.

The crystalline and amorphous substances in the urinary sediment have been described above and illustrated on pages 190-201; the description of the organized sediment follows.

Organized Urinary Sediment

Leucocytes appear in small numbers in normal urine. If they are present in abundance the urine is cloudy. This find-

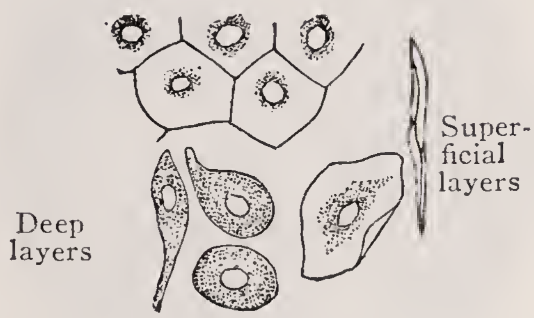


Fig. 63.—Epithelium from bladder, ureters, and renal pelvis.

ing indicates an inflammatory or purulent process in some portion of the urogenital tract (gonorrhœa, cystitis, pyelitis, nephritis), the more accurate localization of which often demands further investigation. With jaundice the leucocytes in the urinary sediment sometimes contain fine crystals of bilirubin.

With chronic gonorrhœa the urine contains fine shreds of mucus, sometimes mixed with leucocytes, occasionally intracellular gonococci, even though the original infection has taken place years before. These mucous shreds are discharged from the prostate or posterior urethra.

Red blood corpuscles are present in the sediment with the most various hæmorrhagic conditions in the urogenital tract (see hæmaturia, page 207). With bleeding from the kidney they are, in part at least, contained in red-blood-cell casts (Fig. 64). In urine of low specific change to gravity red blood corpuscles may appear pale and swollen, and sometimes spherical.

Cells of renal epithelium are small, round or cuboid with a vesicular nucleus. They are usually poorly preserved and often filled with fat droplets. Such cells are sometimes packed together in the form of casts or accumulated upon the outside of casts (epithelial casts, Fig. 64). The presence of renal epithelium is indicative of a pathological process in the kidney. With fatty degeneration of the tubular epithelium large numbers of fat-filled epithelial cells may appear in the sediment. In certain degenerative processes in the renal tubules these fat droplets may be shown to be doubly refractile when examined with polarized light. Under these

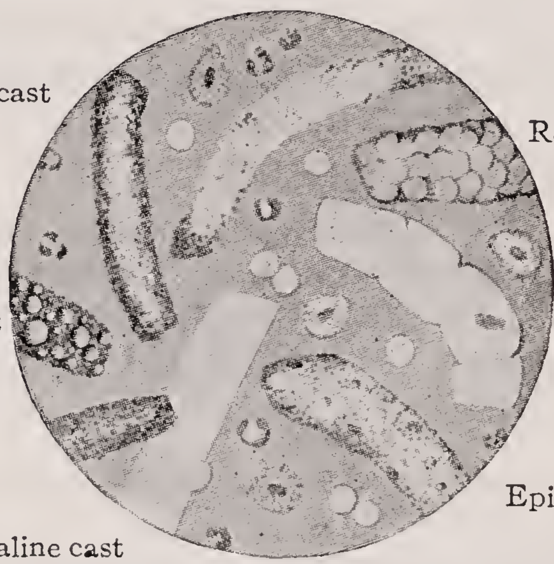


FIG. 64.—Urinary casts.

circumstances the fat droplets appear as bright crosses.

Epithelial cells from the bladder, ureters or renal pelves are indistinguishable from each other. Those from the superficial layers are flat and polygonal, from the deeper layers round or irregular in contour (pear-shaped) and contain a vesicular nucleus. With an inflammatory process involving the bladder or upper urinary passages large numbers of such epithelial cells, accompanied by leucocytes, are to be found in the sediment. It is, therefore, impossible by microscopic examination alone to ascertain exactly which portion of the upper urinary tract may be diseased.

The vagina and præpuce are covered with pavement epithelium similar to that of the buccal mucous membrane.

The male urethra is lined with cylindrical epithelium. Gonorrhœal pus sometimes contains such cells but is distinguished particularly by the presence of gonococci.

Casts are formed in the renal tubules. They occur in large numbers in acute nephritis and in chronic nephritis with œdema, and less profusely with the contracted kidney and with those forms of albuminuria associated with circulatory failure or fever. With icterus bile-stained casts may be observed. In severe cases of diabetes mellitus large numbers of coarsely granulated casts are sometimes found in the urine.

The following types of casts are distinguished:

Hyaline casts which consist of a homogeneous transparent substance and are often indistinct in outline. These are present not only with renal disease proper but with other forms of albuminuria, e.g. febrile diseases, exercise, and jaundice, and are therefore of less diagnostic significance than the other types of casts.

Granular casts with finely granular matrix, are otherwise similar to hyaline casts. They occur, however, almost exclusively with true renal disease, i.e., with acute or chronic nephritis. All stages of transition may be found from granular to epithelial casts.

Waxy casts are refractile, often yellowish, with a distinct contour which is sometimes irregular. They are met with chiefly with **chronic** renal disease and indicate a more severe degree of renal involvement.

Epithelial casts are made up of desquamated epithelial cells from the renal tubules; the cells themselves are seldom well preserved but are usually partially broken down and sometimes have undergone fat necrosis until they appear as granular masses. Single cells of renal epithelium are often observed attached to the outside of hyaline or granular casts. Epithelial cell casts are always indicative of degeneration of the epithelium of the renal tubules.

Red-blood-cell casts represent masses of red blood cells closely packed together. They are a sign of bleeding in the kidney itself. Inasmuch as parenchymatous bleeding in the kidney usually takes place in the Bowman's capsule and arises from the glomeruli the appearance of such casts in the urine may be taken as evidence of glomerulo-nephritis.

Tabular Review of the Principal Renal Diseases

	Urinary Output	Specific Gravity	Appearance	Albumin	Sediment	Functional Impairment	Œdema	Tendency to Uræmia	Heart	Blood Pressure	Blood Rest-Nitrogen (N.P.N.)
Disease of Glomeruli (Glomerulonephritis)	+ or Normal	Medium	Cloudy Bloody	+ to ++++	R.B.C.+ R.B.C.– Casts	Nitrogen Excretion	Seldom	+	Sometimes enlarged	+	+
Disease of Tubules (Tubularnephropathy or Nephrosis)	– or Medium	Medium to high	Usually cloudy and yellow	++++	Casts+ + Epithelium+ R.B.C.– –	NaCl excretion (N excretion Normal)	Usually Present	o	Not enlarged	Normal	Normal
Glomerulo-Tubular Renal Disease (Mixed Types)	– or Medium	Low and fixed	Usually cloudy yellow	+++	R.B.C.+ Casts ++ Epithelium +	NaCl, Nitrogen both impaired	Usually Present	+	Usually enlarged	+	+
Contracted Kidney with Renal Insufficiency	Increased	Low Fixed	Clear	Trace	Occasional cast	N excretion (NaCl normal)	o	++	Greatly enlarged	++	+
Arteriosclerotic Renal Disease without Renal Insufficiency	Normal	Low Normal	Normal	+	o	o	o	o (Apoplexy)	Enlarged	+	o
Chronic Passive Congestion from Venous Stasis	– – –	High Normal	Clear Dark	+ to +++	Few casts R.B.C.+	NaCl excretion impaired	+	o	Diseased	–±	High normal
Renal Disease from Urinary Obstruction (Prostatic Hypertrophy, hydronephrosis, etc.)	++	Low	Colorless	–	W.B.C.++ Bacteria±	NaCl, N Excretion slightly impaired to severely so	Rare	++	Occasionally enlarged	+	+

Hæmoglobin casts are composed of brownish granules of blood pigment. They occur, together with hæmoglobinuria, in certain conditions in which the blood corpuscles are destroyed and their hæmoglobin set free into the blood stream, e.g., after poisoning with potassium chlorate and other poisons, as well as with paroxysmal hæmoglobinuria and black-water fever (in malaria after the administration of quinine). They are occasionally seen following fracture of a long bone and more rarely in severe infectious diseases.

Leucocyte casts are masses of white blood cells which appear with inflammatory disease of the kidney which in turn is usually the result of an ascending infection from the renal pelvis or of a metastatic infection.

Cylindroids are long, irregular masses of mucus and are of no diagnostic significance.

Very frequently other formed elements collect upon the outside of casts: crystals, fat droplets, red blood cells, leucocytes, epithelial cells and bacteria.

Microörganisms may always be demonstrated in specimens of urine which have stood for any length of time. It is, therefore, advisable to search for bacteria only in a freshly voided specimen or still better in one which has been obtained by means of a sterile catheter. With cystitis and pyelitis bacteria, usually B. coli communis, are found; more rarely staphylococci, streptococci and pneumococci. In foul-smelling urine B. proteus vulgaris is sometimes present, a short variable rod, which liquefies gelatine.

In some cases in the absence of demonstrable cystitis, a faintly acid, somewhat cloudy and foul urine is voided which is rich in bacteria. This "bacilluria" is usually caused by colon bacillus and may persist for some time following cystitis or pyelitis. Under normal circumstances the freshly voided urine is bacteria-free. In certain infectious diseases (e.g., sepsis, typhoid and relapsing fever) cocci, typhoid bacilli, and spirilla may be voided in the urine and demonstrable by culture. In tuberculosis of the urogenital tract **tubercle bacilli** are to be found in the urinary sediment. A drop of the sediment obtained by centrifuging a large volume of urine is placed upon a slide, allowed to dry and stained by the method described in the chapter on microörganisms (in case the sedi-

ment does not stick fast to the slide a little dilute egg albumin may be added). With **smegma** of the præpuce or labia, bacilli may appear which, in morphology and staining reactions, are extraordinarily similar to tubercle bacilli. In order to avoid this confusion it is advisable to examine a catheterized specimen of urine. In suspected renal tuberculosis it is possible to establish whether the disease is unilateral or bilateral only by catheterization of the ureters and by examination of the urine from each kidney. If tubercle bacilli cannot be demonstrated microscopically the sediment may be injected into a guinea pig. Even though only a few tubercle bacilli be present the pig usually dies within four to six weeks and, on autopsy, shows the characteristic lesions of tuberculosis.

Tests of Renal Function

For the quantitative estimation of renal function and its impairment in disease several methods have been proposed, some of which involve the measurement of the ability of the kidney to excrete a substance not normally formed in the body:

Dilution test: The patient is directed to drink 1200 c.c. of water and the urinary output is followed for several hours thereafter. Normally the entire volume of water is excreted within the succeeding four hours and the urine shows during this time a low specific gravity (1.005). If water excretion is impaired 200 c.c. or less may be eliminated in the four hours; the specific gravity may not fall below 1.010. In certain types of renal disease, and with circulatory failure the excretion of water is delayed or considerably diminished.

Concentration test: Following his usual evening meal—with no more than 200 c.c. fluid—the patient should neither eat nor drink until the test is over. Urine voided before the patient goes to bed is discarded. Each voiding during the night, and the urine passed on awakening in the morning, is collected separately. At one and two hours after awakening the patient voids again; each specimen in a separate bottle. Normally the specific gravity of at least one of these specimens will be 1.020 or above.

Phenolsulphonphthalein test of Rowntree and Geraghty: One c.c. of an alkaline solution of phenolsulphonphthalein

(containing 6 mg.) is injected intravenously and the urine is collected hourly. Each specimen is then made strongly alkaline and the intensity of the red color after dilution to one liter, is measured in a colorimeter. The colorimeter standard is made up of a solution of a dye containing 6 mg. per liter. The normal kidneys excrete from 60 to 90% of the dye within two hours after injection. With many severe forms of renal disease the phenolsulphonphthalein output is delayed or diminished. In milder forms it may be unimpaired.

Young and Shaw[1] have emphasized the fact that this test will yield most accurate information if urine collections are made at frequent intervals. In the normal individual 25–40% of the dye is excreted within 15 minutes after injection, 50% during the first half-hour, and 60% or more during the first hour. In some instances of renal disease, although the total excretion of phenolsulphonephthalein in two hours may be within normal limits, this may be delayed, so that 20% or less is excreted within the first half-hour.

Clinically it is often observed that in different forms of renal disease the excretion of the various substances usually thrown off in the urine may be unequally affected. Thus, for example in nephritis with œdema, the excretion of salt and water is impaired while nitrogen excretion may be normal. With glomerulonephritis and particularly with a contracted kidney, while salt and water excretion may be normal, the nitrogen output may be conspicuously impaired and may lead to nitrogen retention in the blood.

It is to be noted that various substances are normally concentrated to varying degree in the course of their excretion by the kidney: thus urea is normally concentrated sixty-five fold whereas chlorides are concentrated less than twofold. The substances which tend to accumulate in the blood with impairment of renal function are those which undergo greatest concentration by the kidney. (Ed.)

In certain cases of renal disease there may be a disturbance in the creatinine excretion and, as is also true in gout, a diminution in the output of uric acid. To test the ability of the kidney to excrete these various constituents the patient may receive carefully weighed diet consisting of milk, eggs,

[1] Shaw, E. C.: Jour. Urol., 1925, 13, 575

bread and cheese, and to administer, upon certain days, either urea 20g m., sodium chloride 10 gm., or creatinine 1.5 gm. (or uric acid as sodium urate 1.0 gm. intravenously). The quantitative examination of daily specimens of urine makes it possible to determine the rate and completeness of the excretion of these substances. In every case of renal disease dilution and concentration tests should be carried out, the blood pressure and blood nitrogen should be followed and, the elimination of phenolsulphonephthalein should be tested, preferably by the fractional method mentioned above. (Ed.)

In order to determine which kidney is affected or whether the disease involves the parenchyma or only the renal pelvis it is sometimes necessary to resort to ureteral catheterization. By means of a cystoscope a small catheter is passed into the ureter and through it the urine may be obtained from each kidney separately. These specimens are then examined microscopically for red or white blood cells and bacteria. The ability of each kidney to pass a concentrated urine as well as its power to excrete a dye may be tested by this method.

The intravenous injection of phenolsulphonephthalein is normally followed by appearance of the dye at the ureteral orifice within 3–5 minutes. In the presence of renal disease, or following obstruction to the lower urinary tract this "appearance time" may be greatly delayed. With improvement or following relief of the obstruction it tends to shorten to or toward the normal value. (Ed.)

ANALYSIS OF PATHOLOGICAL CONCRETIONS

Urinary Stones. The stone is crushed to a fine powder and a small specimen heated upon a platinum or porcelain plate. If the specimen is completely burned and leaves no ash (or very little) it may be assumed that the stone is made up of organic substances: uric acid, ammonium urate, xanthin or cystine.

To demonstrate **uric acid** the **murexide** test is applied. A specimen of the powder is mixed in a small porcelain vessel with a drop of nitric acid and slowly heated over a flame to complete evaporation. In the presence of uric acid there remains an orange-red spot upon the vessel, which becomes

purple upon exposure to ammonia gas. Uric acid stones are usually yellowish-red and hard.

To test for **ammonium** the powder is dissolved with dilute hydrochloric acid and filtered. The filtrate is made alkaline with potassium hydroxide and heated in a test tube. There develops, with this procedure, the odor of ammonia; a piece of moist red litmus paper held in the fumes over the mouth of the tube is turned to blue and about a glass rod, moistened in hydrochloric acid, there develops a cloud of ammonium chloride. If uric acid and ammonium are demonstrable the stone contains ammonium urate; such stones are usually pale yellow and fragile.

If neither of these substances is present the powder is tested for **xanthin:** A specimen is dissolved in dilute hydrochloric acid and evaporated upon a small porcelain vessel; if the residue is lemon-yellow in color and does not change upon exposure to ammonia gas but becomes reddish-yellow upon treatment with potassium hydroxide, xanthin is present. Xanthin stones are usually brown in color and hard. They occur rarely.

To test for **cystine** a specimen is dissolved in ammonia by heating. Upon cooling regular hexagonal crystals of cystine may be demonstrated under the microscope. Cystine stones are usually smooth and not extremely hard.

If the stone does not burn completely but is merely discolored by heat it is composed of inorganic substances or of compounds of certain organic acids (uric acid or oxalic acid) with alkalis or alkaline earths.

A specimen of the powdered stone is treated with dilute hydrochloric acid; if the mixture effervesces carbonates are present. If the specimen does not completely dissolve even after heating the residue may contain uric acid (demonstrable by the murexide test). The mixture is filtered, the filtrate is made alkaline with ammonia and then slightly acid with acetic acid; a white precipitate, insoluble even after heating, indicates the presence of calcium oxalate. This mixture is again filtered and the filtrate treated with ammonium oxalate; in the presence of calcium there develops a white precipitate. The mixture is then warmed, filtered and treated with ammonia; the development of a precipitate (of am-

monium-magnesium-phosphate) indicates the presence of magnesia and phosphoric acid. If no precipitate appears the solution is divided into two portions, to the first of which is added sodium phosphate and to the second magnesium sulphate; the appearance of a precipitate in the first test denotes the presence of magnesium, and in the second test phosphoric acid. Phosphoric acid may also be demonstrated in the nitric acid solution by the addition of ammonium molybdate: yellow precipitate.

Calcium oxalate stones are usually very hard, mulberry-shaped and deeply stained with blood pigments; they are insoluble in acetic acid but dissolve in mineral acids without the formation of gas. If a portion be heated at high temperature calcium carbonate is formed, which effervesces upon the addition of acid. Stones composed of calcium phosphate and ammonium-magnesium-phosphate are usually white, soft and friable. Calcium carbonate stones are white and chalk-like.

Intestinal Concretions (fæcoliths) consist of various organic substances mixed with inorganic salts: ammonium-magnesium-phosphate and alkaline sulphates. For purposes of analysis they may be dissolved in hydrochloric acid and examined by means of the procedure described for urinary stones.

Salivary Stones usually are made up of calcium carbonate.

Gall-Stones consist chiefly of cholesterine and bilirubin compounds with calcium. To test for cholesterine the powdered stone is dissolved in warm alcohol and filtered; angular rhomboid plates of cholesterine crystallize out from the filtrate upon cooling. If the cholesterine is, now, dissolved in chloroform and treated with concentrated sulphuric acid, there develops a beautiful cherry-red tint which gradually changes to blue and then to green. To test for bilirubin the residue is made faintly acid with hydrochloric acid and extracted with chloroform while gently warmed; upon the addition of fuming nitric acid there appears the Gmelin reaction.

FLUIDS OBTAINED BY PARACENTESIS

Effusions may be formed in the various body cavities due either to inflammation (**exudate**), to circulatory stasis, or to injury to the lining membrane (**transudate**).

Transudates are almost always serous, seldom sanguinous and, depending upon where they arise, vary in specific gravity from 1.008 to 1.015. **Exudates** are the result of inflammation and may be serous, sero-purulent or sanguinous. Exudates show, in general, higher specific gravity than transudates. It may, therefore, be assumed that a fluid, wherever obtained, is inflammatory in nature if its specific gravity exceed 1.018 (pleuritis, peritonitis). Such a fluid, on the other hand, is to be regarded as a transudate if its specific gravity be less than 1.015.

Inasmuch as the content, in exudates and transudates, of ash extractives etc. is only slightly different, and the protein content alone varies over considerable limits, the **specific gravity** is, in reality, dependent upon the protein content of these fluids. This may be calculated approximately from the specific gravity by the formula of Reuss:

$$E = \frac{3}{8}(S - 1000) - 2.8$$

wherein E represents the protein content in percent and S the specific gravity. With a specific gravity, for example, of 1.018 one may calculate from this formula a protein content of 3.95%. The specific gravity of such fluids should be measured at room temperature since it varies one degree (hydrometer scale) for each three degrees centigrade.

Serous exudates may also be distinguished from transudates by the fact that the former show a precipitate or clouding upon the addition of several drops of dilute acetic acid, due to the presence of a globulin-like protein (test of Runeberg and Rivalta).

Soon after its withdrawal from the body there forms, in a serous exudate, a more or less heavy clot of fibrin, which, upon microscopic examination, is usually found to contain leucocytes and swollen, often vacuolated endothelial cells. To obtain an accurate leucocyte count in such fluids a specimen should be drawn into a small quantity of sodium citrate to prevent clotting. Serous exudates which are formed in the course of a chronic, and particularly in a tuberculous process, contain, in the sediment, white blood corpuscles with round nuclei, of the type of small lymphocytes. In purulent exudates, on the other hand, which are formed as a result of

acute inflammation, e.g., after pneumonia, polymorphonuclear leucocytes predominate. These differences in the leucocyte content are of great diagnostic significance. It is advisable to obtain a specimen of the exudate immediately after its removal and to examine the sediment obtained by centrifugation after staining with methylene blue or by Pappenheim's method. Such effusions as develop in association with malignant neoplasms (carcinoma, sarcoma, endothelioma), show, upon microscopic examination, a mixture of endothelial cells, with lymphocytes, polymorphonuclear leucocytes, red blood corpuscles and tumor cells. Simple, non-inflammatory transudates, on the other hand, show, in addition to the absence of fibrin and the failure to precipitate protein after the addition of acetic acid, relatively few white blood corpuscles.

Purulent exudates show, upon microscopic examination, large numbers of leucocytes (almost exclusively polymorphonuclear forms) which, in old pus, are degenerated and partly broken down. In addition to these there are found, under these circumstances, fat in droplets and crystals, cholesterine plates, and occasionally **Charcot-Leyden crystals.**

Chylous, i.e., milky exudate in the peritoneal cavity occurs particularly with carcinomatous or tuberculous disease of the peritoneum. The milky appearance is produced by the presence of fat which is finely dispersed.

Serous exudates, particularly those from the pleura, are in the majority of cases **bacteria-free.** They may show, upon culture or animal inoculation a few streptococci or pneumococci or tubercle bacilli in tuberculosis.

Purulent exudates, particularly those which have recently accumulated, **usually contain microörganisms.** Peritoneal exudates may contain colon bacilli, staphylococci and streptococci, or gonococci. With empyema streptococci occur in about half the cases. Streptococcus empyemata developing in the course of puerperal fever, erysipelas, scarlatina, influenza or occasionally in tuberculosis, contain thin, flocculent pus and in general run an unfavorable course. Empyemata developing after lobar pneumonia usually contain pneumococci or rarely streptococci. Pneumococcus empyema is characterized by thick pus and usually has a more favor-

able prognosis. Of the two forms, streptococcus empyema heals more slowly and tends more frequently to recur. In tuberculous empyemata, tubercle bacilli may often be demonstrated either alone or mixed with streptococci. Foul exudates, often green in color and having a very nauseating odor, e.g., with lung gangrene, are usually rich in bacteria among which are found various saprophytic forms. Hæmorrhagic exudates are met with particularly in carcinomatosis or tuberculosis of the pleura and are usually of grave prognostic significance. They may sometimes occur with a hæmorrhagic diathesis.

The contents of an **echinococcus cyst** are usually clear, neutral or alkaline, of low specific gravity (1.009 to 1.015), contain no protein, or only traces thereof, but large quantities of sodium chloride and sometimes of glucose and succinic acid. This latter is demonstrated by shaking the fluid with ether after concentrating by heat and acidifying with hydrochloric acid. After the evaporation of the ether, succinic acid remains in crystalline form and, when dissolved in an aqueous solution of ferric chloride, forms a rusty colloidal precipitate of succinate of iron. Upon heating in a test tube succinic acid forms an irritating vapor. Microscopically the fluid from such a cyst shows, usually but not always, characteristic hooklets. In old echinococcus cysts are found crystals of cholesterine and hæmatoidine. In the purulent contents of hydatid cysts in the liver, bilirubin imparts to the pus an ochre-yellow color.

The contents of an **hydronephrosis** are usually transparent, of a specific gravity from 1.010 to 1.020, usually contain blood, pus, and varying amounts of protein and urinary constituents. Since these substances may also appear in echinococcus cysts the diagnosis of hydronephrosis is sometimes to be made with certainty only after the demonstration of large quantities of urea and uric acid. Urea is demonstrated as described on page 190, and uric acid by treating the fluid with hydrochloric acid and examining under the microscope the crystals which are formed. Microscopically, hydronephrotic fluid sometimes contains the round or pear-shaped cells of the epithelium of the renal pelvis.

The contents of **ovarian cysts** are usually mucoid and

yellow, but may be either watery or thick. The specific gravity varies over wide limits (1.003 to 1.055). The fluid contains protein and pseudo-mucin; the latter causes the mucoid consistency. Pseudo-mucin is precipitated neither by acetic acid (in contrast with mucin), nor by heat nor nitric acid. It is, however, thrown down in flakes by alcohol. Upon heating with mineral acid, pseudo-mucin is broken down with the formation of a reducing substance.

In order to demonstrate pseudo-mucin the fluid is freed of protein by the action of heat and acetic acid. In the presence of pseudo-mucin the filtrate is opalescent and mucoid. Upon the addition of alcohol in excess there appears a white flocculent precipitate, which is then isolated and heated with 5% hydrochloric acid until a brown color appears. This mixture is then made alkaline with sodium hydroxide, treated with a few drops of copper sulphate solution and boiled. If pseudo-mucin be present yellow cuprous oxide is precipitated. The demonstration of pseudo-mucin is not of great diagnostic significance since, on the one hand, it may not be demonstrable in all ovarian cysts, and on the other it may sometimes be present in ascitic fluid. Microscopically cells of cylindrical and ciliated epithelium may sometimes be demonstrated as well as colloidal masses.

To ascertain whether a given specimen of fluid obtained by abdominal paracentesis represents ascites or the contents of an ovarian cyst it may be mixed in a test tube with 1/3 its volume of sodium chloride. The appearance of a flocculent precipitate of protein speaks against the origin of the fluid in a cyst and for ascites.

FLUID OBTAINED BY LUMBAR AND SUB-OCCIPITAL PUNCTURE

By means of lumbar puncture the cerebro-spinal fluid may be withdrawn from the sub-arachnoid space about the spinal cord. The method of procedure (Quincæ) is as follows: With the patient lying horizontally upon one side the skin is thoroughly cleansed with tincture of iodine and alcohol and a sterile hollow needle is introduced into the subarachnoid space between the third and fourth lumbar vertebræ. The fourth lumbar vertebra may be distinguished by the fact that it is crossed by a line drawn between the two posterior

iliac spines. The needle should be introduced in the midline pointing directly forward and slightly cephalad. A graduated glass tube is connected to the needle by means of a rubber tube, making it possible to measure directly the spinal fluid pressure by observing the height to which the fluid rises in the glass tube. A pressure greater than 200 mm. of water is to be regarded as abnormal. The pressure appears considerably higher if the lumbar puncture is performed with the patient sitting upright and should, therefore, be estimated only with the patient lying down. The spinal fluid pressure undergoes a transient elevation if the patient coughs or bears down. With conspicuous increase in pressure, e.g., with meningitis, the fluid may spurt out through the needle. A definite elevation of pressure occurs upon compression of both venæ jugulares, as at the same time there occurs a transient stasis of blood in the brain. If a rise in the fluid level of the manometer, i.e., an increase in the fluid pressure in the subarachnoid space about the lumbar cord, fails to occur with coughing and jugular compression it may be assumed that the free communication between the cerebral ventricles and the intracranial subarachnoid space, on the one hand, and the subarachnoid space of the lower spine on the other, has in some way been interrupted, e.g., by a tumor, by pressure from without, or by meningeal adhesions.[1]

It is advisable to withdraw the spinal fluid slowly and only in such amounts as are required for examination (from 2 to at most 5 c.c.). For therapeutic purposes, in the presence of increased spinal fluid pressure, not more than 20 c.c. (in children 5 to 10 c.c.) should be withdrawn and the pressure should never be lowered below 100 mm. In the presence of suspected brain tumor, lumbar puncture is to be avoided since, under these conditions, alarming symptoms may ensue.

For **suboccipital puncture** the needle is introduced just

[1] An interruption of the continuity of the subarachnoid space may also be demonstrated by the introduction of a few c.c. of lipiodol solution into the intracranial subarachnoid space by suboccipital puncture. In the absence of an obstruction this iodine-containing fluid sinks rapidly and may be recognized under the fluoroscope as a dark shadow in the lower lumbar or sacral regions. In the presence of an obstruction in the subarachnoid space, e.g., with spinal cord tumors, disease of the vertebræ, or meningeal adhesions the lipiodol is stopped at the point of obstruction and serves to mark it in an X-ray photograph.

above the upper margin of the spinous process of the epistropheus through the ligamentum nuchæ along the arch of the atlas to the foramen magnum and through the dura into the cisterna cerebello medullaris.

Under normal conditions the cerebro-spinal fluid is water clear, and it may also have this appearance in certain pathological conditions. With meningitis it is usually cloudy or even flocculent, or it may form a delicate web-like film in which cells and, if they be present, microörganisms, e.g., tubercle bacilli, are ensnared. With tumors of the spinal cord the spinal fluid is often yellow in color.

The spinal fluid in the normal individual contains a small number (not more than 6 per cu. mm.) of mononuclear cells. A higher lymphocyte count (20, 50 or more) occurs with syphilitic and meta-syphilitic disease of the central nervous system and its membranes, e.g., tabes dorsalis, and also with certain non-syphilitic processes, e.g., multiple sclerosis. In the acute forms of meningitis the cell content of the spinal fluid is so great as to cause it to appear macroscopically cloudy. With tuberculous meningitis, as well as with tuberculous disease of the vertebræ, the cells are almost exclusively lymphocytes, while with non-tuberculous, purulent meningitis polymorphonuclear neutrophilic leucocytes preponderate.

The cell count of the spinal fluid should always be performed upon a freshly aspirated specimen. The leucocyte pipette is filled to the first gradation with 1% acetic acid (to which has been added 2 c.c. concentrated alcoholic solution of gentian violet per 300 c.c. of solution). The pipette is then filled with the spinal fluid, the mixture is shaken and the cell count determined in a hæmocytometer. In order to determine whether the cells are predominantly lymphocytes or polymorphonuclear leucocytes the fluid may be centrifuged and the sediment stained after drying on a slide. Of particular importance is the bacteriological examination of the fluid. In tuberculous meningitis tubercle bacilli may frequently be demonstrated; in purulent cerebrospinal meningitis either the pneumococcus or the meningococcus intracellularis (see page 336), more rarely streptococci, staphylococci, bacillus typhosus, etc. For bacteriological examination it is advisable to isolate, whenever possible, the delicate film which forms in the

CEREBROSPINAL FLUID IN DIFFERENTIAL DIAGNOSIS

After Fremont-Smith & Ayer: Journal American Medical Association 1927, *89*, 1078

Disease	Initial Pressure: mm. of Spinal Fluid Horizontal Position	Rise on Jugular Compression	Appearance	Cells per cmm.	Globulin	Protein mgm./100c.c.	Sugar mgm./100c.c.	Chlorides (as NaCl) mgm./100c.c.	Non-protein Nitrogen mgm./100c.c.	Gold Sol	Comment
NORMAL											
Normal: Lumbar Cisternal Ventricular	70–190	Prompt	Clear Colorless No Clot	0–5 0–5 0–3	0	15–45 10–25 5–15	50–75 50–75 55–80	720–750	12–18	0000000000	Sugar and chloride values apply to fasting nonfebrile individuals.
Blood plasma	–	–	–	–	–	6,200–8,200	70–110	570–620	18–30	–	
Meningismus	+	N	N	N	O	N or Low	N or +	N or Low	N	N	Large amount of fluid with relatively slight drop in pressure.
INFECTIONS OF THE CENTRAL NERVOUS SYSTEM											
Acute Purulent Meningitis	+	N	Clear to Purulent Faint Yellow + Clot ±	+	+	+	Low	Low	N	Variable	Sugar may be but slightly decreased at outset. Often falls rapidly to under 10 mgm. Chlorides rarely below 640 unless septicemia is present. Meningococci and influenza bacilli found in smear and culture with difficulty; pneumococci, streptococci and staphylococci easily found. Indol present in influenza meningitis.
Acute Anterior Poliomyelitis	+	N	Slight Opalescence Rarely Turbid Faint Yellow ± Delicate Fibrin Web ±	+	Slight +	Slight +	N or Slight Increase	N or Slight Decrease	N	Variable	In Preparalytic Stage PMN may exceed 80%—rapid change to mononuclears. With gradual decrease in cells protein increases for two to three weeks.
Tuberculous Meningitis	+	N	Opalescent to Turbid Faint Yellow ± Delicate Fibrin Web	+ Mononuclears	+	+	Low	Very Low	N	Variable	Excess fluid. Excess PMN very early and in infants. Chloride usually below 640 mgm./100 c.c. Progressive fall in sugar which may be high at outset, to under 30 mgm./100 c.c. or lower. Tubercle bacilli found in clot or sediment, guinea pig inoculation positive.
Encephalitis Lethargica	N	N	N	N or Slight Increase No PMN	±	N or Slight Increase	N or Slight Increase	N	N	Variable	Sugar is normal unless blood sugar is elevated. Over 50% of cases have normal cell count, which rarely exceeds 60 cells. Protein increase when present is slight—rarely reaching 100 mgm./100 c.c.
Brain Abscess	+	See Brain Tumor	Clear and Colorless to Turbid Clot ±	+	±	Slight Increase	N or +	N	N	Variable	PMN nearly always present. If complicated by septicemia or high fever chlorides may fall to low levels. (Brain abscess represents one form of "Aseptic Meningitis.")
Multiple Sclerosis: Clinically Active	N or Low	N	N	Slight Increase (Rarely over 30)	Slight Increase	Slight Increase	N	N	N	Strong Reaction Paretic or Luetic	A strong paretic or luetic Gold Sol reaction in presence of negative Wassermann in patient not previously treated for syphilis is strong evidence for multiple sclerosis.
Multiple Sclerosis: Clinically Inactive	N or Low	N	N	N	N	N	N	N	N	N Weak Paretic or Luetic	
Lateral Sinus Thrombosis	+	Delayed or Absent to Jug. Comp. on Affected Side	N to Turbid Slight Yellow Color or Clot Rare	Usually Slightly Increased	N	N or Low if Uncomplicated	Increased or N	Low or N	N	Variable	Considerable normal variation on the two sides to unilateral jugular compression in many normal individuals. A prompt response on each side excludes complete lateral sinus thrombosis.
Uremia	+	N	N	N	N	N or Low if Uncomplicated	+	May be Increased or Decreased	Increased	Variable May Give Strong Paretic Curve	
CENTRAL NERVOUS SYSTEM SYPHILIS											
Acute Syphilitic Meningitis	+	N	Clear to Turbid Faint Yellow ± Fibrin Clot	+	+	+	N or Slightly Low	Slightly Low	N	Strong Reaction Zone Variable	Wassermann reaction nearly always positive.
"Meningo-Vascular Syphilis"	±	N Rarely Delayed	N Rare Fibrin Clot	+	+	+	N	N	N	Variable	Wassermann reaction nearly always positive.
Progressive Parenchymatous Syphilis	+	N	N Rare Fibrin Clot	+	+	+	N	N	N	Paretic or Luetic	Wassermann reaction always strongly positive. (Includes Tabes, Paresis and Optic Atrophy.)
Late Inactive Forms	N	N	N	N	N	±	N	N	N	Weak Luetic ±	Wassermann reaction weakly positive or negative.

SPINAL SUBARACHNOID BLOCK (TUMOR, POTTS DISEASE, MENINGITIS, ETC.)

Partial Block	Lumbar	N or Low	Delayed	N or Faint Yellow Clot Rare	±	+	+	N	N	N	Variable	Partial block is best demonstrated by combined cistern and lumbar puncture.
Partial Block	Cisternal	N	Prompt	N	±	N	N	N	N	N	Variable	Lipiodol arrest, but some passes by the block.
Complete Block	Lumbar	Low or N	Absent	Colorless with slight clot, to deep yellow with massive coagulation	±	++	+++	N	Slightly Low	N	Variable	Little fluid obtainable. Rapid drop in pressure to zero.
Complete Block	Cisternal	N	Prompt	N Faint Yellow Color or Clot Rare	±	±	±	N	N	N	Variable	Cistern puncture not necessary to demonstrate block. Lipiodol completely arrested.
Tumor of Cauda Equina	Lumbar (below tumor)	Low	Absent or Delayed	Colorless with slight clot, to deep yellow with massive coagulation	N	++	+++	N	–	–	Variable	
Tumor of Cauda Equina	Lumbar (above tumor)	N	Prompt	Yellow or Colorless, Clot ±	N	+	++	N	–	–	Variable	
Tumor of Cauda Equina	Cisternal	N	Prompt	N Yellow Color or Clot Rare	N	±	±	N	–	–	Variable	
Radiculitis of Cauda Equina Also Numerous Cases of Acute Polyneuritis		N	N	N or Yellow Clot ±	±	+ to ++	+ to +++	N	N or Slightly Low	N	Variable	Radiculitis of cauda equina difficult to distinguish from tumor, unless puncture is below lesion and block can be excluded. Lipiodol valuable.

BRAIN TUMOR

Above Tentorium — Not Involving Wall of Ventricle	Lumbar	+	N	N	N	N or Slight Increase	N or Slight Increase	N or +	N	N	Variable	Tumors involving optic chiasm may give increased cells (mononuclears). Lumbar puncture in patients with choked discs may be dangerous unless ventricle is tapped at the same time.
Above Tentorium — Not Involving Wall of Ventricle	Ventricular	+	N	N	N or Slight Increase	N	N	N or +	N	N	N	Ventricular fluid is normal.
Above Tentorium — Involving Wall of Ventricle	Lumbar	+	N	N Occasionally Faintly Yellow	N or Slight Increase	+	+	N or +	N	N	Variable	Protein increase here comes from ventricle.
Above Tentorium — Involving Wall of Ventricle	Ventricular	+	N	N Occasionally Faintly Yellow	N or Slight Increase	+	+	N or +	N	N	Variable	Protein increase occurs in lateral ventricle invaded by tumor—other ventricle may have normal fluid.
Below Tentorium — Intracerebellar and Fourth Ventricle	Lumbar	+	N or Delayed	N	N	Slight Increase or N	Slight Increase or N	N or +	N	N	Variable	Fourth ventricle tumors usually do not cause any protein increase. The protein increase below intracerebellar gliomas is slight, usually under 100 mgm./100 c.c.
Below Tentorium — Intracerebellar and Fourth Ventricle	Ventricular	+	N	N	N	N	N	N or +	N	N	N	Ventricular fluid is normal. Subtentorial block is best demonstrated by combined ventricular and lumbar puncture.
Below Tentorium — Extra-cerebellar	Lumbar	+	N or Delayed	N or Faintly Yellow Rare Clot	N	+	+	N or +	N	N	Variable	Protein increase in these cases is well marked. Usually 150 mgm./100 c.c. or higher.
Below Tentorium — Extra-cerebellar	Ventricular	+	N	N	N	N	N	N or +	N	N	N	Ventricular fluid is normal.

MISCELLANEOUS

"Bloody Tap" (Normal Fluid)	N	N	Blood Tinged or Bloody Supernatent Fluid Colorless or Pink Clot	No Excess of WBC	±	Slight Increase	N	N	N	Variable	Progressively less bloody in consecutive tubes. Supernatent fluid never yellow (at original puncture) even after standing. If much blood is present clot will form.
Early Subarachnoid or Ventricular Hemorrhage (within 24 hours)	+	N	Bloody + Supernatent Fluid Faintly Yellow No Clot	Slight Excess of WBC usually PMN Many Crenated RBC	Slight Increase	Slight Increase	N	N	N	Variable	All tubes equally bloody. Yellow tint to supernatent or centrifuged fluid appears within 2 to 4 hours after hemorrhage occurs, and deepens.
Late Subarachnoid or Ventricular Hemorrhage (up to 2 weeks)	±	N	Bloody ± Supernatent Yellow No Clot	Excess of Mononuclears RBC Crenated	Slight Increase	Slight Increase	N	N	N	Variable	Yellow color will increase for 8 to 12 days, when all RBC usually have disappeared. Compare with Froin Syndrome.
Original "Froin Syndrome"	Low or N	Absent	Deep Yellow Clear, Massive Coagulation	+	++	+++	N	Slightly Low	N	Variable	See "Complete Spinal Subarachnoid Block"—above. Distinguish from late subarachnoid hemorrhage by high protein content.

fluid after standing. Bacteria may sometimes escape discovery in the lumbar spinal fluid although they are present in the inflamed meninges; this is particularly true of meningococci. These organisms may frequently be demonstrated only by methods of concentration and culture: 5 c.c. of freshly aspirated spinal fluid are mixed in the test tube with 1 c.c. of sterile glucose solution or ascitic broth and incubated in the dark for 12 hours. Under these circumstances meningococci in large numbers, many of them contained in leucocytes, may often be demonstrated. In addition to meningitis an increase in the amount and pressure of the spinal fluid may take place with tumors, hæmorrhage and other diseases of the brain. With hæmorrhage in the brain or spinal cord the fluid is usually bloody.

The **Wassermann reaction** may be carried out upon the spinal fluid according to the method described on page 328. With **general paresis** the Wassermann reaction may be negative in both blood and spinal fluid, in **syphilis of the brain** the blood Wassermann is often negative and that in the spinal fluid positive, with **tabes dorsalis** the spinal fluid Wassermann is positive in the majority of cases while the blood Wassermann is not infrequently negative.

The cerebro-spinal fluid shows an extremely low **protein content:** From 0.06 to 0.18%. The protein content of the blood is, compared with that of the fluid, very high, (about 400 to 1). Spinal fluid which has become contaminated with blood in the process of withdrawal is, therefore, unsuitable for any accurate determination of the protein content. The protein of the cerebro-spinal fluid is composed of almost equal parts of albumin and globulin. A protein content of over 0.2% is to be regarded as pathological. Very delicate tests are required, particularly in the presence of low-grade chronic disease of the meninges, to demonstrate an increased protein content. Most sensitive is the sulpho-salicylic acid test or the Heller's ring test which makes possible the demonstration of as little as 0.03% protein. The fluid is diluted 5 times with physiological saline solution and this mixture is carefully layered above pure nitric acid. Any fluid is to be considered abnormal if, in this dilution, it forms a ring at the interface of the acid within one minute.

The **ammonium sulphate** test (Nonne-Apelt) is positive with a protein content above 0.5%. One c.c. of spinal fluid is mixed with an equal volume of a concentrated aqueous solution of ammonium sulphate. The development of clouding or of a flocculent precipitate is evidence of a considerable protein (globulin) increase and is indicative of severe meningeal involvement.

With all **acute** diseases of the meninges, which are associated with an increased permeability of these membranes, certain constituents of the blood (erythrocytes, leucocytes and above all blood protein) pass over into the spinal fluid, and in these conditions, in contrast to the more chronic meningitides, there occurs in the spinal fluid a conspicuous elevation of the albumin content in addition to an increase in the cellular elements and a relatively slight increase in globulin.

Upon such small amounts of fluid as are generally available quantitative determination of albumin and globulin is often difficult. A relatively simple method, in the hands of individuals who have practised it, is the **goldsol reaction** of C. Lange:

Ten small test tubes are set up in a row and beginning with No. 2, 1 c.c. of an 0.4% salt solution is added to each. In the first tube there are mixed 1.8 c.c. of 0.4% salt solution and 0.2 c.c. of spinal fluid, giving a dilution of spinal fluid of 1:10. From this dilution 1 c.c. is pipetted into the 2nd tube; after thorough mixture 1 c.c. is pipetted from the 2nd tube into the 3rd and so on through the series of tubes until one obtains a series of spinal fluid dilutions from 1:10 to 1:5000. To each tube there is now added 5 c.c. of a colloidal gold solution obtained by Zsigmondy's method by reduction with formaldehyde in a solution made alkaline with potash.

The reaction is empirically so arranged that, in the presence of the normal protein content of the fluid, the ruby red color of the goldsol remains unaltered throughout the entire series of dilutions. With an increased protein content changes are observed in the color of the mixture or sometimes precipitation of gold, the **degree** of which is dependent upon the absolute concentration of protein. The **point** in the series at which the maximal reaction takes place is determined by the relative proportion of globulin to albumin. With a high

globulin content the maximum reaction occurs in the first tubes (i.e., in the lower dilution), with a high albumin content in the higher dilutions of the last tubes.

The sugar (glucose) content of the cerebro-spinal fluid reflects that of the blood except in the presence of inflammation in the central nervous system or meninges. It varies normally between 80 and 100 mg. per 100 c.c.; in acute meningitis it may fall to 30 mg. per 100 c.c. In epidemic encephalitis it is usually elevated.

The cerebrospinal fluid normally contains 700–750 mg. chlorides per 100 c.c. These are reduced (to 600 mg. or lower) in tuberculous meningitis, and to a lesser degree in acute purulent meningitis or poliomyelitis.

PERSONAL NOTES

PERSONAL NOTES

CHAPTER VI

GASTRO-INTESTINAL TRACT AND ABDOMINAL ORGANS

MOUTH

One examines particularly the condition of the buccal mucous membranes, of the gums, and the tongue: Tongue coated in febrile diseases as well as in certain gastro-intestinal diseases (not with ulcer or carcinoma); tongue dry and often cracked in very ill patients who breathe with the mouth open. Smooth tongue in pernicious anæmia not infrequently associated with painful inflammation of the buccal mucous membranes and gums. Lingual mucous membrane may be smooth and atrophic with long-standing syphilis. Thrush, which may be present in severe infectious diseases or in debilitated individuals (seldom in the normal mouth) appears as white plaques the size of the head of a pin or larger over the buccal mucous membranes and gums. Aphthæ, small, painful, white epithelial defects, with a red zone about them, are not to be confused with thrush.

In **scurvy,** due to "avitaminosis," the gums are spongy, swollen, livid in color, drawn away from the teeth, and tend to bleed easily.

TEETH

The milk teeth consist of 20 teeth; 2 incisors, 1 canine and 2 molars on each side of each jaw. The milk teeth erupt between the seventh month and second year of life. The first to appear are the median inferior incisors (6th to 8th month). Then follow the remaining 6 incisors (7th to 9th month). Next come the upper and lower anterior molars (12th to 15th month), then the upper and lower canines (16th to 20th month), and finally, at the end of the 2nd year, the posterior molars. In the 7th year of life the milk teeth fall out in approximately the same sequence in which they first erupted and the permanent teeth appear.

The permanent denture consists of 32 teeth, on each side

of each jaw 2 incisors, 1 canine, 2 premolars, and 3 molars. The first to appear are the anterior molars, which erupt during the 4th or 5th year of life posterior to the posterior premolars of the milk teeth. In the 7th year there follow the median incisors, first the lower and then the upper. In the 9th to the 10th year appear the anterior premolars, in the 10th to the 11th year the canines, and in the 11th to 12th year posterior premolars. The second, or middle, molars make their appearance in the 12th or 13th year of life and between the 16th and 20th years appear the posterior molars or wisdom teeth.

In rickets the first dentition is delayed; the teeth remain small and are often notched at their edges. In hereditary syphilis the upper incisors of the permanent teeth are shortened and their biting edges hollowed out in a half-moon shape. The lower incisors may at the same time be narrow and pegged. These characteristic changes in the teeth (Hutchinson's teeth) constitute one member of the **Hutchinsonian** triad: Deformation of the permanent teeth, interstitial keratitis, and deafness. Defects in the dental enamel occur as a result of rickets and together with cataract and tetany in hypoparathyroidism.

Infection at the roots of the teeth may sometimes lead to systemic infection, i.e., to the picture of chronic sepsis. It is, therefore, necessary in any septic condition to rule out infection at the base of the teeth: Rœntgenograms show rarefaction of the bone about the root of the affected teeth, due to a so-called granuloma.

In **pyorrhœa alveolaris** pus accumulates in the dental alveoli under pressure and exudes between the base of the teeth and the swollen, inflamed gums. The teeth themselves are not necessarily diseased but, due to the persistent inflammation at their bases, become loosened and may eventually fall out. The patient loses one tooth after another in this fashion. This disease seems prone to occur in families, particularly in those showing diabetic or gouty diathesis.

SALIVA

Normal saliva has a specific gravity of 1.002 to 1.006; reaction is normally alkaline, but, with processes of decomposition

in the mouth, and occasionally in diabetes mellitus, may be acid. The saliva contains only traces of protein and occasionally, though not always, of potassium thiocyanate (KCNS). This is demonstrated by the addition to the saliva of several drops of hydrochloric acid and dilute ferric chloride. There appears, in the presence of KCNS, a bluish-red color. In the saliva there is also diastatic ferment, ptyalin, which converts starch into dextrin and maltose.

The diastatic action of the saliva continues following the swallowing of the food, which has been masticated and thereby thoroughly mixed with saliva, for a considerable period after it reaches the stomach, but is inhibited as soon as the concentration of hydrochloric acid has reached a certain level (0.12%). To demonstrate the salivary ferment a small quantity of saliva is mixed, in a reagent glass, with a dilute solution of starch and allowed to stand at body temperature. After a few minutes maltose is formed and may be recognized by Trommer's test. By the demonstration of diastase and of KCNS it is possible sometimes to say with certainty whether a given specimen of expectorated material really contains saliva.

ŒSOPHAGUS

The length of the œsophagus in the adult is about 25 cm. Eight cm. from its beginning it is crossed by the left bronchus. The distance from the upper incisor teeth to the beginning of the œsophagus is about 15 cm. When, therefore, a stomach tube has been passed for more than 40 cm. (measured from the upper incisor teeth), one may assume that it has reached the stomach. If, on the other hand, the tube meets with an obstruction, one may measure the distance from the upper incisor teeth to the tip of the tube and thereby ascertain at what point in the œsophagus the obstruction lies. Thus, for example, if the tube has passed in only 23 cm. it is to be assumed that the stricture is at the point at which the left bronchus crosses the œsophagus. Stenosis of the œsophagus is usually associated with carcinoma, more rarely with scar tissue resulting from swallowing lye or acid. If the sound sometimes encounters an obstruction while at other times a large sound passes unobstructed into the stomach, there

exists, presumably, a spasm or, more rarely, an œsophageal diverticulum. Narrowing of the œsophagus can also be recognized by means of auscultation: posteriorly just to the left of the spine, or over the stomach in the costal angle just below the xiphoid process. Shortly after swallowing there is a spurting, splashing sound followed by another similar sound several seconds later (primary and secondary murmur of deglutition). This murmur is delayed or diminished in stenosis. The material which collects above an œsophageal stenosis or in a diverticulum and which may, from time to time, be discharged, may be differentiated from vomitus by the absence of an acid reaction and of pepsin.

Stenosis or dilatation of the œsophagus, foreign body, and diverticula may best be demonstrated by transillumination with X-ray: the thorax is illuminated obliquely so that the posterior mediastinal space, lying in front of the spine and behind the heart, is brought into view. The course of the œsophagus may then be made visible by having the patient drink 400 c.c. of milk, in which sufficient barium sulphate or bismuth subcarbonate has been stirred to form a thin paste. One may thus follow the course of the opaque material after it is swallowed throughout the entire œsophagus, and, in the case of obstruction, may observe a delay or collection at the point of narrowing.

In the diagnosis of diseases of the œsophagus and in particular for the demonstration of foreign bodies, œsophagoscopy is useful. A straight metal tube about the size of the finger is passed through the mouth and into the œsophagus, while the head of the patient is bent backward. (Caution with suspected aneurysm of the aorta!)

ABDOMEN

The abdomen under normal conditions is soft, is nowhere tender to pressure, and produces a loud tympanitic note on percussion. Such loops of intestine as are filled with fæces or contracted, and therefore air-free, particularly in the left flank in the region of the descending colon, may give a dull note upon percussion. With regard to the X-ray examination of the intestines see page 257.

The abdomen appears **sunken** or **scaphoid** if the intestinal

canal is empty, i.e. with long-standing fasting or with stenosis of the œsophagus or cardia, or if the loops of intestine are strongly contracted as may be the case with lead colic or meningitis.

Distension of the abdomen occurs:

(1) With distension of the intestines by large quantities of gas (**meteorism**), which may occur in typhoid, intestinal catarrh, especially in children, often in peritonitis, and is particularly severe in partial or complete intestinal obstruction. With excessive gaseous distension of the small intestine the abdomen may be barrel-shaped or dome-shaped. Abnormal amounts of gas in the large intestine tend usually to collect in the region of the hepatic and splenic flexures.

(2) With **peritonitis** the abdomen is tense, usually distended, and exquisitely tender to pressure. Hiccoughing and vomiting also occur with small, easily compressible pulse and rapid loss of strength. In localized peritonitis, e.g. as a result of ulceration and perforation of the appendix, the tenderness is usually confined to the diseased portion of the abdomen. With appendicitis there is often a tender point or area midway between the anterior superior spine of the ilium and the umbilicus (McBurney's point). Over the inflamed area one may sometimes feel and hear a peritoneal friction; particularly is this true in perisplenitis or perihepatitis.

If **perforation of the stomach or intestine** takes place, e.g. with gastric ulcer, with typhoid ulcer or appendicitis, or with gun-shot wound of the abdomen, there ensue the stormy manifestations of severe peritonitis: Diffuse tenderness of the abdominal wall which is at first flat and board-like, and later extreme abdominal distension, hiccoughing,[1] vomiting, suppression of intestinal peristalsis and therewith of the passage of flatus and stools, small, soft, very rapid pulse, and rapidly developing weakness. If, with such a perforation, air escape into the abdominal cavity the air bubble always assumes the uppermost position so that, dependent upon the position of the patient, the hepatic or splenic dulness may give place to a loud tympanitic note.

[1] Persistent, uncontrollable hiccough is not only observed in conditions causing irritation of the diaphragm but is also met with in many cases of irritation of the phrenic nerve, mediastinitis, carcinomatous metastases in the mediastinum, etc.

(3) With **intestinal obstruction,** which may result from strangulation in a hernia, from kinking or twisting of the bowel (particularly as a result of old peritoneal adhesion), from intussusception or carcinoma, there develops the picture of ileus, the more rapidly the higher the obstruction: Exaggerated peristaltic movements, fæcal vomiting, rapid loss of strength, and small, rapid pulse. If the obstruction lie high up in the intestine the urinary secretion is suppressed, if it be in the lower ileum or colon the urinary secretion is increased and the urine contains large quantities of indican. One of the most important signs of intestinal obstruction is the suppression of stool and flatus, a finding which is sometimes met with also in peritonitis or appendicitis.

In every case of intestinal obstruction it is important that both the **inguinal canals** and the **rectum** be examined by palpation.

(4) Distension of the abdomen may be caused by **an accumulation of fluid within the abdominal cavity (ascites).** This may be part of generalized anasarca, e.g. as a result of nephritis or heart failure. Ascites alone, in the absence of œdema over the sacrum or extremities, is due either to stasis in the domain of the portal vein or to an inflammatory effusion into the peritoneal cavity.

With **portal stasis,** which may be caused by atrophic cirrhosis of the liver, by chronic passive congestion of the liver in cases of heart failure or adhesive mediastinitis, more rarely by syphilis of the liver or portal thrombosis, with the patient in the dorsal position the abdomen bulges conspicuously in the flanks and is flat in the region of the umbilicus (frog belly); with the patient upright the abdomen is dependent or pendulous. The upper border of dulness, corresponding to the upper level of the fluid, is horizontal and freely movable, shifting when the patient is turned from side to side.

Peritoneal exudate, in contrast with those transudates described above, is often encapsulated; its outline is irregular and changes little or none with change in position of the patient. With chronic peritonitis, usually caused by tuberculosis or carcinoma, in contrast to acute peritonitis, the abdomen may be only slightly tender.

(5) With **tumors** of the abdomen the abdominal wall bulges irregularly; with tumors of the liver and spleen in the upper portion, and, with tumors arising in the pelvis, in the lower portion. Ovarian tumors produce, in common with the pregnant uterus, an area of dulness extending upward from the pelvis having a convex upper margin; percussion in the flanks gives, under these conditions, the normal loud note. Fæcal masses lying in the course of the colon are distinguished by the fact that they are compressible, that they change their position, and, with evacuation of the bowel, disappear. If a tumor of the large intestine, or a stenosis of the same, cannot be localized by palpation and percussion it is sometimes advisable to fill the colon with air by means of a tube inserted in the rectum; it is often useful to fill the stomach with water at the same time and to determine its position by percussion. Obstruction in the colon may best be localized by fluoroscopic examination during the administration of a barium enema. In any case of abdominal tumor rectal examination, and, in women, pelvic examination should never be omitted.

Palpation of the abdomen is only of value if the abdominal wall be relaxed. To this end it is sometimes necessary to place the patient in a warm bath or in some cases to resort to narcosis. In palpating over the stomach one searches first for circumscribed areas of **tenderness** which may indicate the presence and location of an ulcer, and second for **tumors** which, particularly when hard or nodular may be carcinomatous. Tumors of the stomach show little or no up and down movement with respiration, in contrast with tumors of the liver and spleen.

With a thrusting type of palpation in the region of the stomach a splashing noise may sometimes be elicited. This is occasionally noted in the normal individual shortly after ingestion of food or drink in considerable quantities, but is most striking in cases with atony of the stomach wall. When it is present several hours after the last meal, that is, at a time when the normal stomach should be empty, it is a sign of delayed evacuation. If this splashing noise is met with over a larger area than is normally occupied by the stomach,

e.g. below the umbilicus or to the right of the midline, it speaks for gastroptosis or for dilatation of the stomach.

STOMACH

Under normal conditions, with the patient in the dorsal position, the empty stomach assumes the shape of a cow-horn, the broadest portion of which is represented by the fundus and the tip by the pylorus. The fundus, i.e., pars cardiaca, lies just beneath the left dome of the diaphragm, and the pylorus slightly to the right of the midline a little below the tip of the xiphoid process. The greater curvature lies immediately beneath the ribs, and below them, next to the anterior abdominal wall, and runs in a curve from behind and above forward and downward. The œsophagus opens into the stomach through the cardia on the median side of the fundus. When filled, and in the upright position, the stomach does not assume this shape but hangs like a tubular sac from the dome of the diaphragm downward into the abdominal cavity and the pylorus no longer represents the deepest point (vertical position, fish-hook, or siphon-shaped stomach, see Fig. 20, page 65). In its first portion (i.e., the bulbus) the duodenum rests against the pylorus like a cap; the second portion, after a sharp bend, passes downward to the right of the spine behind the peritoneum and receives the pancreatic and bile ducts through a common opening in the papilla of Vater; the third portion bends to the left, and lies posterior to the stomach passing over into the jejunum. If the stomach is considerably lengthened, so that the greater curvature extends well below the umbilicus, one speaks of **gastroptosis.** In such cases the lesser curvature does not lie, as under normal conditions, entirely behind the left lobe of the liver, but it is also pulled down and may sometimes be visible as a curved depression beneath the anterior abdominal wall. **Gastroptosis** is often combined with descent of the kidneys, liver, spleen, and colon and this condition is known as **enteroptosis** or **Glenard's disease. Gastroptosis** is not to be confused with **gastrectasia** or dilatation of the stomach, in which this organ undergoes not only a lengthening but also a considerable and persistent enlargement.

The shape, position and size of the stomach as well as its

motility may best be studied by **fluoroscopy.** For this purpose one may use the meal of Rieder (300–400 gm. of mush, rice or potato, to which has been added 30–70 gm. of bismuth subcarbonate or 100 gm. of chemically pure barium sulphate). This meal casts a sharp shadow under the X-ray and makes it possible to outline accurately the contours of the stomach.

Berg has pointed out the advisability of visualizing the folds of the gastric mucous membrane by the administration of a small quantity (tablespoonful) of the opaque meal, and, by means of massage and change of position, causing it to cover the stomach wall. Upon fluoroscopy the folds of mucosa may then be seen in their characteristic arrangement. With mucosal thickening, i.e., in cases of chronic gastritis, the folds are widened while with scar formation they may be seen to radiate from a central depression.

The upper portion of the stomach is occupied by an air bubble representing the air swallowed with the food. With the patient in the upright position this bubble lies beneath the dome of the left diaphragm. The stomach wall is normally contracted against the contents by the tone of the circular musculature (peristole). This peristaltic contraction is less pronounced in the atonic stomach. In the fundus, under normal circumstances, only superficial peristaltic waves are seen. In the pyloric portion, on the other hand, the peristaltic contractions are strong, separate this antrum pyloricum from the upper portion of the stomach and progress downward against the pylorus; whereupon the pylorus opens and allows a portion of the stomach contents to pass out into the duodenum. Carcinoma is to be recognized in the X-ray picture by irregularities in contour of the stomach shadow or by insufficiency of peristalsis in the pyloric portion. Scar formation following a gastric ulcer may produce a localized constriction, the so-called hour-glass stomach. Anti-peristalsis is observed in the stomach only with organic disease of the stomach or duodenum, and is due to obstruction.

An ulcer on the lesser curvature not infrequently leads to a contraction of the musculature of the greater curvature on the opposite side, producing a deep furrow in the wall of the stomach. This type of contraction is periodic and transient

in contrast to the persistent stricture of the genuine "hour-glass" stomach which is produced by a localized cicatricial narrowing of the stomach lumen. A deeper ulcer, the base of which lies in the muscularis, the serosa or, after perforation through the entire stomach wall, in the perigastric tissue, produces often a crater-like diverticulum from the stomach. This sign, the so-called Haudek's niche, is pathognomonic of gastric ulcer.

Since bismuth or barium sulphate are not absorbed the movement of the opaque meal may be observed under the fluoroscope as it passes from the stomach through the small intestines and into the colon. Under normal conditions the meal has left the stomach in the course of from 3 to at most 6 hours. It passes much more rapidly through the small intestines and within 3½ to 5 hours appears in the cæcum where it gradually accumulates. After 5 to 8 hours it is visible in the hepatic flexure of the colon, and after 7 to 12 hours in the splenic flexure. In the descending colon there is normally very little delay so that in from 8 to 15 hours after ingestion the meal has accumulated in the sigmoid flexure and rectum.

In order to mark out the size of the stomach by **percussion** one determines first the position of the diaphragm and the borders of the liver and splenic dulness. Between these organs one encounters the deep tympanitic note of the stomach which contrasts sharply with the high-pitched tympanitic note of the intestines. This localization is at best inaccurate since, by percussion, it is only possible to delimit the air in the stomach which may or may not represent the entire stomach lumen. The upper portion of this area of tympany, bounded above by the lung borders, on the right by the left margin of the liver, on the left by the splenic dulness, and below by the costal margin, is called the **semilunar space of Traube.**

If the stomach be distended by a meal, or by directing the patient to drink quickly two glasses of water, its lower border may be percussed accurately with the patient in the upright position. Under these conditions the lower portion of the stomach is represented by an area of dulness which may be sharply marked off from the note of the intestine

and which, when the patient assumes the dorsal position, gives place to a loud tympanitic note.

TESTS OF GASTRIC FUNCTION

Physiological Considerations

Under fasting conditions the stomach is entirely empty or contains at most a few c.c. of a weakly acid fluid. The moment that food is taken the secretion of gastric juice commences. Its secretion is excited by a variety of stimuli: 1. under the influence of the appetitie, e.g. by the sight, taste, smell or even by the thought of food; 2. under the influence of the act of mastication; 3. by the action of certain foods, e.g. meat or meat extract of soups, directly upon the mucous membranes. The gastric juice shows normally a rather constant acidity of .03 to .05% HCl. Almost immediately upon secretion the hydrochloric acid is bound by proteins and other basic constituents of the food and appears in excess or free only when these possible combinations are saturated. If the gastric contents be aspirated 45 minutes after breakfast or 3 to 5 hours after the midday meal, they are found to contain 0.1 to 0.25% HCl, or calculating from the entire volume of the gastric contents, 0.1 to 0.6 gm. HCl. During digestion, in addition to HCl, the stomach also secretes **pepsin** and a **rennet-like** ferment. The former, in the presence of an acid reaction, brings about the solution of protein and splits it to form albumoses and peptone; the latter causes the casein of milk to clot. Both ferments appear in the stomach in the form of inactive precursors (zymogens) from which they are liberated or activated by the action of HCl. Very little absorption takes place through the gastric mucous membrane; water is absorbed not at all, sugar and alcohol only in small quantities. Soon after the ingestion of food there begins the rhythmic evacuation of the gastric contents through the pylorus in small spurts. As a result only a small quantity of chyme is present in the duodenum at any one time. Water is evacuated with the greatest rapidity, other fluids require a somewhat longer time. Solid foods remain in the stomach until, by the dual action of the gastric juice and the peristaltic movements of the stomach wall, they are reduced to a semi-fluid consistency. A test breakfast is com-

pletely evacuated from the stomach after 2 hours and a midday meal after 4 to 6 hours.

The rhythmic opening and closure of the pylorus, and thereby the emptying of the stomach, is in reality controlled from the duodenum. With the passage of the acid stomach contents through the pylorus into the duodenum the pylorus is reflexly closed, to remain so until the duodenal contents shall have been neutralized and passed on into the jejunum. For this reason, in cases with gastric hyperacidity, the emptying of the stomach is often delayed.

Tests of Motor Function

Motor function may best be observed by fluoroscopy; or, the stomach contents may be removed in the evening, 6 hours after the midday meal (no food having been taken during the afternoon). If, in the gastric contents so removed, there are particles of food, it may be safely concluded that the evacuation of the stomach is pathologically delayed. The same condition in a more severe grade may be demonstrated by giving a large meal in the evening and aspirating in the morning. In the most severe cases there may be found in the stomach contents or in the vomitus particles of food which have been ingested a day or more previously.

Deficient evacuation of the stomach may be caused: 1. by pyloric stenosis (carcinoma, or cicatrix resulting from gastric or duodenal ulcer); 2. by atony of the gastric musculature as is found in many chronic gastric conditions. Atony of the stomach may also best be demonstrated by fluoroscopy. The gastric contents (opaque meal) in atonic ectasia do not fill the vertical portion of the stomach lumen up to the air bubble but lie in a pool in the lowest portion of the relaxed pouch.

Tests of Chemical Function

Chemical examination of the gastric contents is best accomplished by giving the patient a **test breakfast,** consisting of a roll and either a cup of tea or a glass of water (Ewald), and aspirating 45 minutes later. This test breakfast stimulates gastric secretion only slightly. A more stimulating meal consists of 5 gm. of Liebig's meat extract in 250 c.c. of warm

water with 4 gm. of salt and a piece of toasted white bread. A test meal consisting of a plate of beef soup with noodles, a portion of beefsteak with mashed potatoes, 50 gm. of bread and a glass of water (Riegel), may be given at the usual lunch hour and removed after 3 hours.

The gastric contents may be removed by passing a rubber tube moistened with water or oil into the stomach. A certain amount may be removed by pressure upon the abdomen or contraction of the abdominal muscles. If this is insufficient the remaining portion may be aspirated with a bulb or suction flask.

The reaction of the aspirated gastric contents is first tested with litmus. An acid reaction may be produced by: 1. free HCl, 2. by HCl which is loosely bound with proteins or organic bases, 3. by organic acids, e.g. lactic, acetic, or butyric.

To determine whether free, (unbound) HCl is present several drops of gastric contents are placed in a porcelain dish, an equal quantity of Günzburg's reagent is added (2 gm. phloroglucine, 1 gm. vanillin, 30 gm. alcohol) and the mixture is carefully heated over a small flame. In the presence of free HCl there soon appears a red band at the edge of the fluid. Since Günzburg's reagent is relatively unstable and must often be renewed, it is advisable to dissolve the two constituents of the reagent each in 15 c.c. alcohol and mix these two solutions in equal quantities just before using.

The reaction of the gastric contents may also be tested with various indicators. If several drops of an aqueous solution of congo-red are added to a sample of gastric contents in a test tube the presence of free HCl is demonstrated by a blue color and a bluish precipitate. This reaction may also be produced by certain organic acids (lactic acid) but only in such concentrations as are rarely encountered in the gastric contents. Hydrochloric acid which is bound to protein or organic bases fails to react with this reagent. Filter paper soaked in a congo-red solution may be used in this test (touch the paper with a glass rod previously dipped in the gastric contents). The addition to a sample of gastric juice of several drops of a 5% solution of dimethylaminoazobenzol causes the appearance of a red color which changes to orange in the

presence of free HCl. If, to a sample of gastric contents containing free HCl in normal concentration, one adds several drops of a very dilute solution of methyl violet, the color changes to blue. If free HCl be absent the violet tint remains; with hyperchlorhydria the mixture becomes distinctly blue or even greenish blue. By means of this test it is possible to determine quickly whether one is dealing with an increase or decrease in the HCl concentration.

In addition to HCl and inorganic acid salts, organic acids may also be present in the stomach contents: lactic, acetic and butyric acids among others. These are not secreted by the gastric mucous membrane but are produced during stagnation by the fermentation of the food and particularly of the carbohydrates. Among these organic acids **lactic acid** is by far the most important. This is produced only when no free HCl is present, with stagnation of the gastric contents. It is the product of the action of certain long, non-motile bacteria which may easily be stained with methylene blue. These bacilli are particularly abundant in the gastric contents with carcinoma of the stomach and are to be found in the small clumps of blood which are often mixed with the vomitus or aspirated gastric contents in such cases. Large amounts of lactic acid are found most frequently with gastric carcinoma but may also occur with other gastric diseases. On the other hand lactic acid may be entirely absent in those cases of carcinoma in which free HCl is present in the stomach contents.

Since lactic acid is contained in small quantities in certain foods (meat, sour-milk, bread, sauerkraut), it is sometimes more accurate to wash out the stomach first and then to give a test meal free from lactic acid and to withdraw it several hours later. However, the amount of lactic acid contained in the food is so minute that for the ordinary test it need not be considered.

To test for lactic acid 10 c.c. of filtered gastric contents are shaken with 25 c.c. of ether in a test tube, or better in a small separatory funnel, and allowed to settle. The ether containing lactic acid is then drawn off. To this there is added 5 c.c. of distilled water with 2 drops of a dilute solution of ferric chloride (1:9 aq.) and the mixture is shaken vigorously. In the presence of lactic acid the solution is turned a yellow-green by

the production of ferric lactate. Instead of the dilute ferric chloride solution, Uffelman's reagent may be used (30 c.c. of a 1% solution of carbolic acid to which 3 drops of ferric chloride solution is added just before using). The amethyst-blue color of this mixture is changed to a greenish-yellow in the presence of lactic acid.

Quantitative Estimation of Gastric Acidity

To determine quantitatively the total acidity (which is conditioned by the free as well as the bound HCl and by organic acids and acid salts), 10 c.c. of filtered gastric contents are measured with a pipette into a beaker and diluted with distilled water and mixed with several drops of phenolphthalein solution. Decinormal sodium hydroxide solution[1] is then added from a burette until there appears a red color which persists on stirring. In the place of the phenolphthalein one may use litmus solution, which, however, gives rather lower acid values. The number of cubic centimeters of decinormal sodium hydroxide required for neutralization (persistent red color) measures the acidity and this is then expressed in terms of 100 c.c. of gastric contents. To measure the free acidity in the gastric contents the same technique is used except that in place of phenolphthalein one employs as indicator dimethylaminoazolbenzol (several drops of a 5% solution: color red to orange). It is usually more advisable to titrate in the same sample of gastric contents, first the free HCl with dimethylaminoazobenzol and then, after the addition of phenolphthalein, the total acidity. In case free HCl is absent one may titrate the acid deficit, i.e. determine that quantity of tenth-normal HCl which is necessary to give the reaction of free HCl with congo-red or a similar indicator.

[1] A normal solution contains one equivalent weight of the solute per liter. Thus, since the equivalent weight of sodium hydroxide is 40 (Na = 23, O = 16, H = 1) a normal solution of this substance is made up of 40 gm. dried NaOH per liter of solution and a tenth-normal solution of 4 gm. (The equivalent weight of any substance is the molecular weight divided by the hydrogen equivalent. Since the hydrogen equivalent of sodium is 1, its equivalent and molecular weights are the same and a normal and a molecular solution of NaOH contain identical amounts of the salt. In the case of calcium chloride, however, the hydrogen equivalent of calcium being 2, a normal solution should contain ½ molecular weight per liter.) One c.c. of tenth-normal hydroxide should neutralize exactly 1 c.c. of tenth-normal HCl.

If the gastric contents give a strong reaction for free HCl one may assume that no organic acid is present.

In the normal individual, after a test meal the total acidity is equivalent to 50 to 70 c.c. of tenth-normal sodium hydrate per 100 c.c. gastric contents, and the free HCl, 20 to 45 c.c. After a test breakfast the total acidity is normally 30 to 60 c.c. and the free HCl 20 to 40 c.c. The acidity of normal gastric contents corresponds, therefore, to a concentration of 0.15 to 0.2% HCl. Since the pure gastric juice contains a rather constant concentration of 0.3 to 0.4% HCl it is apparent that the food is normally mixed with an equal quantity of gastric secretion.

If in the gastric contents there are demonstrable larger amounts of acid and particularly of free HCl, i.e. when the titration value of the total acidity is above 70 and of the free HCl above 45 c.c., one speaks of **hyperacidity.** Such a finding always suggests the presence of a gastric ulcer. It is, however, met with from time to time in cases of dilatation of the stomach without ulcer, and sometimes in gastric neurosis. Hyperacidity usually is due to the fact that the food is mixed with an abnormally large quantity of gastric juice (gastrosuccorrhœa), whereas the percentage concentration of HCl in the gastric juice itself is increased very little or not at all. **Gastric hypersecretion** or **Reichmann's disease** is a condition in which acid-containing gastric juice continues to be secreted into the stomach during the fasting state. This may be demonstrated by aspirating the gastric contents in the morning before breakfast. In case motor insufficiency be also present it is usually advisable to wash out the stomach the evening before. Gastric hypersecretion often goes hand in hand with hyperacidity and produces usually more severe symptoms than hyperacidity alone. Not infrequently, however, in cases of hypersecretion, the gastric contents contain only small quantities of acid (gastrohydrorrhœa). In the X-ray picture the abnormally large quantity of gastric juice may sometimes be seen as a semi-opaque layer on top of the opaque meal and may be caused to splash if the patient be shaken.

The periodic secretion of large quantities of strongly acid gastric juice accompanied by severe pain and vomiting and

interrupted by periods of normal gastric function is designated as "paroxysmal gastroxynsia" or "nervous dyspepsia." Similar attacks may accompany the gastric crises of tabes.

If the degree of acidity of the gastric contents be abnormally low one speaks of **subacidity.** In such cases free HCl is absent, indeed an HCl deficit may be demonstrated in that additional HCl must be added to produce an acid reaction to Günzberg's reagent. The absence of free HCl at the height of gastric digestion is in many cases to be explained upon the supposition that only a small quantity of gastric juice, and therewith too little HCl is secreted, e.g. with atrophy of the gastric mucous membrane. In such cases the estimation of the chloride concentration in the gastric contents gives also very low values. In other cases a deficiency of HCl may presumably be due to the presence of abnormally large quantities of the products of protein digestion (albumoses, peptone, amino-acids and bases) which bind the HCl. Under these circumstances the **HCl deficit** may be measured by titrating with tenth-normal HCl against an indicator. While the normal gastric digestion of protein, through the action of pepsin, ordinarily proceeds only to the albumose stage, in the presence of pathological ferments, found sometimes in the secretion of an ulcerating carcinoma, the protein digestion may advance still farther, i.e., to the formation of simple peptids, amino-acids and amino-bases. These end products are able to bind large quantities of HCl and as a result with gastric carcinoma there is often a considerable HCl deficit. The gastric acidity may sometimes be normal in cases of carcinoma or even increased, particularly if the carcinoma has developed upon the basis of an old gastric ulcer. Subacidity also occurs in many forms of gastric catarrh and with atrophy of the gastric mucosa. With the latter condition the secretion of pepsin is insufficient or lacking (achylia gastrica); this occurs frequently in pernicious anæmia.

To determine the efficacy of the gastric juice to digest protein a small amount is placed in each of two test tubes and a flake of fibrin is added to each. To one there are added several drops of 1% HCl and both tubes are then placed in an incubator at body temperature. If, after 6 to 12 hours, the fibrin flake is not dissolved in either tube it is to be concluded that

there is a deficiency of pepsin. If, however, the fibrin is digested only in the tube containing HCl acid the gastric juice contains pepsin but no HCl. With normal gastric juice the fibrin is digested in both tubes after 1 to 2 hours.

In examining for the presence of rennin 10 c.c. of raw milk are placed in a test tube with a drop of filtered gastric juice. In the presence of rennin, clotting occurs within a quarter or a half hour. If no clotting occurs 10 c.c. of milk may be mixed with 3 c.c. of a 5% solution of calcium chloride and a drop of gastric juice. If coagulation occurs under these circumstances the zymogen of the ferment is present. Coagulation takes place more rapidly at body temperature (in an incubator).

Fractional Methods of Gastric and Duodenal Drainage

In place of the withdrawal of a single specimen of gastric juice following a test breakfast or a test meal it has recently become customary to withdraw fractions of the gastric contents through a tube which is allowed to remain in place. This procedure makes it possible to follow the secretory and motor function of the stomach during the entire period of digestion. A long, thin tube of about ½ cm. diameter, with a perforated metal olive attached at its lower end, is introduced into the stomach, preferably in the morning, with the patient in a fasting condition. The tube is passed 45–50 cm. when it may be assumed that the lower end has reached the stomach. Specimens of the gastric contents are withdrawn from time to time by means of a syringe attached to the upper end of the tube. A sample of the fasting contents is first obtained. There is then introduced through the tube one of several stimulating solutions: 100 c.c. of a warm 5% solution of alcohol or 0.2 gm. caffein dissolved in 300 c.c. distilled water. To either solution are added 2 drops of a 2% solution of methylene blue; a small portion is withdrawn at once for comparison with the following fractions. Ten c.c. samples are aspirated at 10 minute intervals and placed in a series of glass vessels. Normally the bluish color disappears within ½ to 1 hour after the administration of the solution. Under pathological conditions this "emptying time" may be shortened or prolonged. After the solution has left the stomach gastric secretion continues for some time and tests may be made upon samples of this after-

secretion during the subsequent hour. The individual fractions are measured, filtered, and titrated for free and combined acid against dimethylaminoazobenzol or phenolphthalein.

The results of such an examination may be plotted, and the form of the resultant curves provides a graphic record of the gastric function. The first fraction commonly shows an acidity somewhat less than that of the fasting contents; this is presumably the result of dilution. Under normal conditions the curves of the free and combined acid run almost parallel and form a semi-circle; the maximum degree of acidity, representing a total acidity of 30–70 and a free HCl of 20–50, is reached within 40–60 minutes, i.e. by the time of the disappearance of the bluish discoloration. A high, steep curve, indicating a total acidity of 80–130 and a content of free HCl of 60–100, is commonly observed with hyperacidity and hypersecretion. These abnormally high acid values usually reach their maximum within 30–40 minutes. They are associated with gastric ulcer, with cholecystitis and with certain conditions of abnormal irritability of the gastric mucosa.

With certain destructive lesions of the stomach, e.g., gastric carcinoma, atrophy of the mucous membrane, pernicious anæmia and other forms of achylia, the total acidity tends to be low (under 30) and there exists, often, a deficit of free HCl. The resultant curves are low and flat and the interval between the curve of total acidity and that of free HCl is particularly striking, corresponding to the negative value of the HCl deficit.

In a similar fashion the examination of the **contents of the duodenum** may furnish information concerning the function of the biliary system and of the pancreas. The same long, thin rubber tube is used; it is passed for at least 45 cm. and the patient is placed upon his right side with the hips somewhat elevated; the tube is then allowed to pass to 75 cm. The position of the metal olive at the end of the tube should be observed by fluoroscopy until one is satisfied that it lies within the duodenum. A further check is the observation of a bile-stained alkaline fraction upon withdrawal. The duodenal contents usually flow spontaneously out of the end of the tube

and may be collected at 5 minute intervals or withdrawn with a syringe. The various specimens are examined microscopically for bacteria (culture) and for the evidences of inflammation (leucocytes). The duodenal contents are normally sterile but in certain pathological conditions microörganisms (streptococci, B. coli, yeast cells or protozoa) may be found. The presence of pancreatic secretion may be demonstrated by testing for trypsin; a sample is placed in a test tube with a bit of fibrin or coagulated egg-white and digestion observed. The presence of bile is indicated by the golden-yellow color of the duodenal contents.

The bile, which is formed in the liver and discharged through the hepatic duct, is commonly a bright yellow. Gall-bladder bile, which has undergone the absorbing and concentrating action of the mucous membrane, is commonly viscous and dark brown. The introduction into the duodenum of olive oil, peptone, or magnesium sulphate, or the subcutaneous injection of pituitrin brings about contraction and emptying of the gall-bladder and the discharge of its contents into the duodenum. This **gall-bladder reflex** may be utilized to test the function of the gall-bladder and, as well, the patency of the cystic duct. With obstruction of this passage by gall-stones this reflex is lost and the characteristic dark, viscous bile is not found in the duodenum; with obstruction of the common bile duct the duodenal contents are not even bile-stained.

[Bloomfield, Keefer et al.,[1] have devised a method which makes possible simultaneous study of motor and chemical function and volume of secretion. Histamine is used as a stimulus.

The subject fasts for at least 12 hours and is examined in bed under standard basal conditions. A duodenal tube is passed for a sufficient distance to allow its tip to reach the most dependent part of the stomach. The patient is urged not to swallow saliva and this point is emphasized throughout the test. As soon as the tube is in place, the fasting contents are withdrawn with a syringe. (A 50 c.c. Luer is most satisfactory.) Continuous aspiration is then begun. After the fasting secretions have been collected over two or three

[1] Bloomfield, A. L. and Keefer, C. S.: J. A. M. A. 1927, **88**, 707.
Bloomfield, A. L. and Polland, W. S.: J. A. M. A. 1929, **92**, 1508.

10 minute periods and have reached a minimum, histamine (0.1 mg. per 10 kgm. body weight) is injected hypodermically to stimulate gastric secretion. After the injection of histamine, aspiration is continued over as many 10 minute periods as desired; the observations are usually stopped within an hour after injection.

Results: The average volume of gastric secretion in normal persons varies from 1.05 to 7.0 c.c. per min. The emptying time of the stomach varies from 20 to more than 90 minutes. The volume of secretion and the acidity of the juice are practically constant on repeated examinations of the same person; motility varies greatly. A study of abnormal cases yields characteristic results in only two types of disorder —gastric ulcer (high volumes, high acid values) and cancer of stomach (low volumes and failure to secrete acid). A study of true cases of anacidity (from pH 6.0 to pH 7.0, failure to secrete acid after histamine) shows the condition to be relatively rare and usually associated with serious organic disorder of the stomach or with pernicious anæmia. Motility of the stomach is found to be very variable after a barium meal as well as after an alcohol test stimulus. Sodium bicarbonate (from 1 to 2 gm.) exercises a quantitative neutralizing effect on gastric acid, but does not stimulate or inhibit gastric secretion. Ed.]

In the diagnosis of gastric disease the patient's story of his symptoms is of the utmost significance:

Gastric pain characteristically occurs regularly at the same time of day and is apparently dependent upon the time at which nourishment is usually taken and upon the kind of food. It appears in hyperacidity and gastric neurosis and is particularly common with pylorospasm, but is most frequently a sign of an ulcerative process: gastric ulcer or carcinoma. The pain appears either immediately following the taking of food, particularly of food which is mechanically or chemically stimulating, e.g. coffee, sour foods or coarse bread, or, as is more usual, makes its appearance when the HCl secretion reaches its maximum. In some cases gastric pain is not present during the process of digestion but occurs only after the stomach has emptied, and disappears on the taking of food. These "hunger pains," which are noted

before meal-time, in the late evening and particularly in the night and early morning, are characteristic of ulcers immediately within the pylorus or in the duodenum. In gastric ulcer the pain is increased in severity if the patient assume a particular position such that the acid gastric contents are brought into contact with the ulcer, e.g. in the right lateral decubitus if the ulcer is at the pylorus. With gastric ulcer there may sometimes be demonstrated a circumscribed area or point, which is very tender upon pressure, or a hyperæsthetic zone in the domain of the 8th to 10th thoracic segments (Head's zone). It is, however, unwise to assume such a circumscribed area of tenderness to be due to an ulcer unless, by X-ray examination, it can be demonstrated that such really lies within the region of the stomach and not outside of it, i.e. above the lesser curvature. Attacks of very severe cramp-like pains appearing at irregular intervals and independent of the kind or time of feeding, popularly known as **cramps** in the stomach, are far more often a sign of gall-bladder or renal colic than of gastric disease. Not infrequently painful contractions of the colon are mistaken for stomach cramps, and are to be distinguished by the fact that they occur in the early morning hours and commonly cease with the passage of stool or flatus. Sometimes, also, the painful sensations of angina pectoris (coronary arteriosclerosis) are confused with gastric pain and particularly when they appear after a large meal. In tabes dorsalis there may occur attacks of most severe gastric pain accompanied by persistent vomiting. These **"gastric crises"** often alternate with periods of absolutely normal gastric function and are sometimes mistaken for gastric disease proper. Gastric pain is to be contrasted with the feeling of fulness and pressure in the region of the stomach so common with catarrh and dilatation of the stomach, with hyperacidity, and especially with gastric neuroses.

Under the term **heartburn, pyrosis,** is described a burning sensation rising up into the neck, which is often met with in the presence of abnormally high gastric acidity.

Eructation of gas occurs with fermentation of the gastric contents and is particularly common with hyperacidity. Such gastric contents continue to ferment after withdrawal,

as may be demonstrated by placing in the fermentation tube. In the upper end of such a tube the gas may be collected. If potassium hydroxide is added to the tube CO_2 is absorbed, with pyrogallol the oxygen (the air which has been swallowed). Hydrogen and methane, the latter sometimes formed from CO_2 in the fermenting gastric contents, burn if ignited. Gaseous eructation is also particularly common (in the absence of gastric fermentation) in hypochondriacs who swallow large quantities of air.

A nauseating odor about the mouth may occur with putrefactive processes in the stomach but usually is caused by disease in the mouth or pharynx (carious teeth, stomatitis, pyorrhœa alveolaris, Vincent's angina), or in the nose (ozæna).

Vomiting may occur with any gastric disease but is absent in many cases. Vomiting shortly after the taking of food is usually a sign of increased irritability of the stomach. Vomiting of large quantities of fermented or putrefied gastric contents, occurring every few days, but seldom daily, is a sign of dilatation of the stomach with stagnation of its contents, and is usually associated with pyloric stenosis. The act of vomiting is controlled from the medulla oblongata by way of the vagus and sympathetic nerves. If a patient complains of persistent vomiting certain conditions are to be considered in addition to intra-abdominal disease. Among these are poisoning, uræmia, pregnancy, intra-cranial disease and abnormal sensitivity of the labyrinth.

Vomitus may contain:

Mucus which is present in large quantities in gastric catarrh.

Saliva, which has been swallowed and which may be identified by the fact that it contains potassium thiocyanate (blue-red color with dilute ferric chloride).

Blood, which may be found in the vomitus with gastric ulcer or carcinoma, melæna neonatorum, cirrhosis of the liver, syphilis of the liver, or sometimes with hæmorrhage from the œsophageal or gastric mucous membranes as a result of severe and persistent vomiting. The blood may be vomited unchanged, or, after remaining for some time in the stomach, may be partially digested to a coffee-like brown

mass. In the latter case the red blood corpuscles are destroyed and the hæmoglobin transformed to hæmatin, which may be demonstrated with the hæmin test. The Weber test is more practical for the demonstration of blood in gastric contents as well as in fæces: A small amount of unfiltered gastric contents (or of stool mixed with water) is placed in the test tube with 1/6 its volume of concentrated acetic acid and a small amount of water and then is shaken in a small separatory funnel with several c.c. of ether. If the ether fails, after a few minutes, to separate out as a clear layer above, a few drops of alcohol may be added. If the ether remain colorless no blood is present. If, on the other hand, the specimen contain blood pigments (hæmoglobin or hæmatin) these are changed through the action of acetic acid into acid-hæmatin which colors the ether a reddish-brown. In order to prove that the discoloration of the ether is caused by hæmatin and not by some other substance a sample of the ether layer is placed in another test tube and several drops of a fresh tincture of guaiac and an equal quantity of hydrogen peroxide are added. If within a few moments there appear an outspoken blue or violet color the presence of blood pigment may be taken as proven. This reaction is more striking if the acid reaction of the ether extract be depressed by the addition of a few drops of sodium hydroxide. A still more accurate test consists in alkalinizing a sample of the ether layer with ammonium hydroxide, adding a few drops of a solution of ammonium sulphate, and examining spectroscopically. The presence of blood will produce the characteristic spectrum of reduced hæmatin (see table of spectra), or at least the first band thereof, in the yellow-green. In order to avoid confusion of this test by the blood content of the food it is advisable to eliminate all meat from the diet for 2 days prior to the examination. If the guaiac test is negative the presence of blood may be taken as excluded and spectroscopic examination as superfluous. In place of the guaiac one may employ **benzidine** in alcoholic solution with a small amount of H_2O_2: blue-green color in the presence of small amounts of blood.

Bile may be found in the vomitus after protracted vomit-

ing due to regurgitation of the duodenal contents. **Pancreatic juice** may sometimes pass upward into the stomach. The regurgitation of bile and pancreatic juice takes place most frequently if large quantities of oil (200 c.c. or more) be introduced into the fasting stomach. Boldireff has made use of this fact in order to gain access to the intestinal contents for examination. The gastric contents are removed a half hour after the administration of oil and examined for the presence of trypsin by testing their action upon protein at an alkaline reaction. It is more practical to determine the presence of bile or pancreatic juice in the duodenum by aspiration through a duodenal tube.

The **food particles** which are present in vomitus are often considerably altered by the process of digestion, or by the action of bacteria. Fermentation and putrefaction result in the breakdown of carbohydrates (starch and sugar) into lactic, butyric and acetic acid, of the neutral fats into fatty acids, and of the proteins into peptone, leucine (tryosine) phenol, indol, skatol, hydrogen sulphide and ammonia. The latter products of putrefaction are only met with in stagnation of the gastric contents, or when the intestinal contents are regurgitated into the stomach and vomited (so-called "fæcal vomiting").

Microscopically there are found in vomitus food particles, e.g. striated muscle fibers, vegetable cells, fat, starch granules, and, in gastric contents which are free of acid and in which the proteolytic function is depressed, large particles of meat. With hyperacidity carbohydrate digestion is impaired and large quantities of starch may be present, as may be demonstrated by the addition of Lugol's solution. Epithelial cells from the mouth or the œsophagus, rarely cylindrical epithelial cells from the gastric mucous membrane, may also be found, and frequently leucocytes, the cytoplasm of which has been digested so that only the nucleus remains. Yeast cells and sarcinæ are present in stagnant gastric contents; lactic acid bacilli are particularly common with gastric carcinoma, since the secretion of the cancer is apparently favorable to their growth; but the mere presence of these long bacilli is in no sense pathognomonic of carcinoma.

INTESTINE

Morphological or functional abnormalities of the small intestine are most easily observed by following the movement of ingested material (barium sulphate) which is opaque to X-rays by means of fluoroscopy. The **jejunum** is recognized by the fact that its plicæ circulares protrude into the lumen, causing transverse irregularities in its shadow. In the **ileum** these irregularities are, for the most part, absent. In the transverse colon there appear sacculations corresponding to the haustra. In the hepatic and splenic flexures of the colon accumulations of gas often alter the density of the shadow cast by the opaque meal. The descending colon and sigmoid are often incompletely filled by barium administered by mouth. These portions of the bowel and indeed the entire colon may best be visualized by the X-ray following the injection of barium (Rx. 2%) by enema.

Strictures, stenoses or gross abnormalities of the bowel wall, e.g., carcinoma, may often be recognized by the consequent distortion of the shadow of the barium-filled lumen.

The movements of the intestine (peristalsis) occur automatically under the influence of the nerve plexuses contained in their walls. Peristalsis is augmented by the action of the Vagus and inhibited by the Sympathetic nerves.

Constipation may be caused by: (1). Tonic contraction of the colon, particularly in the transverse portion. Under these conditions the colon is sometimes palpable through the abdominal wall as a cord about the thickness of the thumb. The abdomen in such a case is often tense and upon X-ray examination masses of fæces may be visualized in the transverse and descending colon, separated into single round balls interspersed by transparent contracted segments of intestine. This condition is particularly common in constipation occurring with lead poisoning or with certain nervous diseases. It is also often found with gastric and duodenal ulcer. It may best be treated with belladonna. (2). By abnormally sluggish peristalsis in the colon (atony). In the X-ray examination it may be seen that the opaque meal lies for several days or a week in the ascending and transverse, more rarely in the descending, colon, often accompanied by an accumulation of

gas. (3). By delay in the emptying of the ampulla recti: In these cases the intestinal contents pass through the upper portion of the colon at the normal speed and fæcal material accumulates in the rectum, producing conspicuous dilatation of the ampulla. On rectal examination large fæcal masses may be felt, whereas under normal conditions the rectum is empty, since, as soon as fæces begin to accumulate in the ampulla recti, evacuation takes place and the column of fæces in the descending colon is usually passed at the same time. This form of constipation, which is dependent upon deficient function of the rectum alone, is designated as dyschezia (Herz) and yields to treatment by enemata. On the other hand, constipation resulting from atony of the upper portions of the colon is best combated by the use of a coarse diet which leaves considerable residue and by certain forms of exercise. (4). Insufficient evacuation of the bowel is observed in stenosis of the intestines, frequently caused by carcinoma or tuberculosis of the colon and rectum, more rarely by cicatricial stricture as a result of syphilis, tuberculosis or dysentery, or with strangulation of the bowel by peritoneal adhesions. Under these conditions the portion of the bowel lying above the obstruction tends to dilate and to show abnormally strong contractions. The passage of the intestinal contents through the stenosed area may sometimes be audible as a distinct murmur. (5). The passage of both fæces and gas may be impaired in acute peritonitis and appendicitis, because, as a result of the peritonitis, the colon and the small intestines may be paralyzed. Irregular, intermittent, obstinate constipation occurs with congenital dilatation of the colon **(Hirschsprung's disease).**

Diarrhœa occurs, aside from certain nervous disorders and as a result of catharsis, in all conditions which involve stimulation or inflammation of the intestinal mucous membrane: e.g., with bacterial putrefaction of the intestinal contents, with acute intestinal catarrh, with all ulcerative lesions of the intestines (typhoid, dysentery, tuberculosis), and also with sepsis and certain gastric diseases. With **chronic intestinal catarrh** there is usually alternating constipation and diarrhœa. Inflammation of the mucosa of the rectum or descending colon, e.g. with dysentery or mercurial poisoning,

produces very painful evacuation (**tenesmus**) and the passage of large masses of bloody mucus with the stools. In many nervous conditions, as well as with hyperthyroidism, diarrhœa occurs as a result of accelerated peristalsis. Persistent, so-called "gastrogenous diarrhœa" is observed in those diseases of the stomach associated with achlorhydria; it may be relieved by prescribing HCl.

Proctoscopy is performed by means of a straight metal tube about the thickness of the thumb (sigmoidoscope) introduced into the rectum. The lumen of the tube is illuminated by an electric lamp. By this means tumors, ulcers, scars or abnormalities of the mucous membrane of the rectum may be visualized up to the angle of the sigmoid.

FÆCES

The fæces are composed of: (1) the remains of food altered by processes of digestion and putrefaction, (2), of the digestive juices poured out into the intestines and, (3), of certain products which are excreted from the organism through glands which open into the intestine, e.g. salts of calcium and of the heavy metals, iron, lead, mercury, etc. In addition the stool contains enormous numbers of various types of bacteria, particularly colon bacilli.

Relative to its **consistency** the stool is described as **firm, semi-fluid,** or **fluid.** The latter type, except as it results from catharsis or from certain types of diet, is not to be considered normal. Fluid stools (diarrhœa) occur if the intestinal peristalsis is accelerated, passing the food so rapidly through the intestines that absorption is incomplete, or more rarely, in the presence of an abnormal secretion or exudate from the intestinal mucous membrane, e.g., cholera or dysentery.

The **color,** as well as the consistency and volume of the stool, is principally dependent upon the **diet.** Upon a diet consisting chiefly of meat dark brown, small, firm stools are passed. With a high starch diet (bread, potatoes) the stool is brownish-yellow, soft, foamy and large. On a pure milk diet it is yellowish-white and firm; with egg diet, yellow and soft; with a chlorophyll-rich diet, brownish-green. In addition the color of the stool may be changed by certain drugs. Following iron or bismuth it is a green-black or black (iron

sulphide or bismuth sulphide), following mercury, particularly calomel, a greenish-brown (bile pigments and mercuric sulphide), following rheum yellowish-brown. Hæmorrhages in the stomach or duodenum (ulcer or carcinoma, hepatic cirrhosis or syphilis, melæna neonatorum), or in the small intestines (typhoid, embolism of the superior mesenteric artery) produce dark red, tarry stools; the blood pigments are altered by the action of digestive juices. If, on the other hand, the bleeding take place in the colon or rectum (dysentery, mucous colitis, carcinoma, syphilis of the large intestine, hæmorrhoids), the blood is passed unchanged and bright red. To test for the presence of blood in the fæces the small mass is mixed with a little water, treated with several c.c. of concentrated acetic acid, shaken with ether and examined according to the procedure described above under gastric contents (page 271, Guaiac test).

Unchanged **bile pigments** rarely appear in the stool under normal conditions. These are usually altered by bacterial action in the intestines and reduced to colorless hydrobilirubinogen, which is subsequently transformed into hydrobilirubin (stercobilin). Only the stools of nursing infants are golden yellow with bilirubin. Unchanged, bile pigments may occasionally appear in the stools as a result of hyperperistalsis, e.g., in typhoid and other forms of diarrhœa. In the enteritis of infants the stools are often green with biliverdin.

If the common bile duct be completely occluded so that no bile reaches the intestines, hydrobilirubin is absent from the stools, since this is formed in the intestines by the reducing action of bacteria upon the bilirubin of the bile. Failure to demonstrate hydrobilirubin in the stools is proof of the absence of bile in the intestines; in such cases urobilin and its precursor are absent from the urine. To test for the presence of hydrobilirubin in the stool a small portion is mixed with a concentrated alcoholic solution of zinc acetate and filtered. In the presence of hydrobilirubin the filtrate shows a green fluorescence and in the spectroscope a characteristic band between the green and blue (see table of spectra).

If **no bile reaches the intestines,** fat absorption is greatly impaired; the stool contains large quantities of fat and appears, therefore, gray, greasy, clay-colored, and, upon

microscopic examination, shows large numbers of needle-like crystals in tufts. These are composed of calcium soap and melt to fat droplets if the preparation be heated after the addition of a drop of concentrated acetic acid. Upon shaking with water such stools produce a peculiar iridescence. If the normal flow of bile into the intestine be resumed, the stools recover their normal characteristics and color long before the disappearance of jaundice from the skin.

In addition to icterus an impairment of fat absorption and the appearance of **fatty stools** is observed with caseation of the mesenteric lymph glands, in chronic peritonitis, in severe anæmia, as well as in mild enteritis and in amyloid disease of the intestine. (In the severe forms of this latter disease there may be uncontrollable diarrhœa.) Fatty stools are, therefore, not absolute proof of the total absence of bile in the intestines. In some cases of impaired absorption fat appears in the stools, not in the form of the calcium-soap crystals described above, but as fatty-acid, or neutral fat. The fatty-acids form tufts of delicate, bent needles which melt to glistening droplets when the preparation is warm, in contrast with the plump calcium-soap crystals which melt to droplets only after splitting with acid. Neutral fats appear in the stools in the form of fat droplets. If fat, in the form of neutral fat, is predominant in the stools it is a sign that the break-down to fatty-acids and glycerine in the intestines is incomplete. This takes place, among other conditions, in the absence of pancreatic secretion. In severe disease of the pancreas not only the digestion and absorption of fat is impaired, but also the digestion of meat. In such cases not only are large quantities of neutral fat present in the stool but also masses of unaltered muscle fibres, or indeed whole pieces of meat. In the absence of pancreatic secretion it is apparently the digestion of the muscle nuclei which suffers most. The examination of the stool for neutral fats, muscle fibres and nuclei gives, however, only untrustworthy information regarding the presence of pancreatic juice in the intestines.

Mucus is present in the stool in large quantities in mucous colitis, and appears in small clumps in fluid stools with disease of the small intestine. Under these conditions the mucus is discolored with bile and gives, in the microscopic preparation,

the typical Gmelin reaction with nitric acid. With disease of the large intestines large clumps of mucus, discolored with blood, are often passed, which are not mixed with the stool and are easily distinguishable macroscopically. These mucous masses are often passed alone (in dysentery, enteritis or mucous colitis). Large strings or ribbons of mucus may be passed after severe colicky pain.

Pus is found in the stool with any ulcerative process in the large intestine, e.g. with chronic dysentery or tuberculous ulcer, with syphilis of the colon and cancer. Large quantities of pus occur in the stool with perforation of a periappendiceal, perirectal or parametrial abscess into the intestine.

In typhoid the stools may often have the appearance of uncooked pea soup, in cholera they are like rice water, and in dysentery contain blood, pus and mucus.

Upon **microscopic examination** the fæces show remains of food particles and fragments of muscle fibres, which, in the process of normal digestion, have lost their characteristic striations and often their nuclei. The presence of connective tissue in the stools may indicate a somewhat deficient gastric digestion, inasmuch as connective tissue is only digested by the gastric juice and not by the trypsin from the pancreas. Starch granules are never normally present in the stools. Their presence, which may be demonstrated by the addition of Lugol's solution with the appearance of a dark blue color, speaks for deficient digestion in the small intestines. Fat appears normally in small amounts in the form of droplets. When present in larger quantities and in the form of crystals of calcium soaps or fatty-acid, it indicates impaired absorption. On a vegetable diet all sorts of vegetable remains appear in the stools, e.g. spiral fibres, cell membranes, etc. In addition, one occasionally finds in the stool the coffin-shaped crystals of ammonio-magnesium phosphate and the laminated crystals of other calcium salts as well as spear-shaped Charcot-Neumann crystals. These latter occur principally with helminthiasis, e.g. with ankylostomiasis.

The following **cellular elements** may appear in the stool: **Leucocytes** with intestinal catarrh or with ulceration, **red blood corpuscles** with intestinal bleeding. Cylindrical **epithelial cells** sometimes appear in large numbers with intestinal

catarrh. Squamous epithelial cells are derived from the lower rectum and anus.

Microörganisms appear in the stools in enormous numbers; of diagnostic significance is the presence of tubercle bacilli, of typhoid, dysentery bacilli or cholera vibrio. (For methods of isolation and culture see chapter on microörganisms.)

To demonstrate **tubercle bacilli** in the stools a small portion is mixed with about 20 c.c. of water, thoroughly stirred and centrifuged. The upper third of the fluid is drawn off and mixed with two parts of 95% alcohol and again centrifuged. The sediment is then placed upon a slide, fixed and stained for tubercle bacilli.

To demonstrate the **ova of parasites** several small particles of stool are placed upon a slide with a little dilute acetic acid, covered with a cover glass and examined microscopically. Or a specimen of fæces may be thoroughly mixed with 25% antiformin and an equal quantity of ether in a mortar, and centrifuged; the sediment is then examined microscopically. Or, finally, the stool may be mixed with a concentrated aqueous solution of sodium chloride whereupon the eggs rise to the surface and may be found in the superficial layers of the fluid (Fuelleborn).

In order to draw accurate conclusions, from the condition of the stool, regarding functional disturbances of the gastro-intestinal tract it is necessary to place the patient upon a controlled and easily digestible diet, such as that of Schmidt: morning, 500 c.c. milk (or cocoa) with 50 gm. zwieback. Forenoon, 500 c.c. oatmeal gruel with 200 c.c. milk, 10 gm. butter and 1 egg. Noon, 125 gm. scraped beef broiled with 20 gm. butter and 250 gm. mashed potato. Afternoon, 500 c.c. milk (cocoa). Evening, 500 c.c. oatmeal gruel. This diet is administered for three days and the stools of the last day are carefully examined.

PANCREAS

The pancreas has two functions, an external, which consists in the production of pancreatic juice, and an internal whereby it functions as a gland of internal secretion, and has to do with the regulation of the sugar metabolism. Fol-

lowing extirpation of the pancreas, with atrophy of the gland and particularly of the islands of Langerhans, as well as with tumors and hæmorrhages which destroy pancreatic tissue, hyperglycæmia and glycosuria appear and glycogen gradually disappears from the liver. The pancreatic juice, which is poured out through the papilla of Vater into the intestine in quantities up to 600 or 800 c.c. daily, contains three kinds of ferments: Trypsin which, in an alkaline reaction, breaks down albuminous substances (particularly albumoses) into peptones and amino acid, lipase, which splits neutral fats into fatty acids and glycerine, and diastase, which forms maltose and glucose from starch. These ferments, particularly the trypsin, are not secreted in their active form, but as proferments, which are activated only after contact with the duodenal mucous membrane (by the enterokinase contained therein). The secretion of the pancreatic juice is stimulated through "secretin," formed by the action of hydrochloric acid upon the duodenal mucous membrane. The presence of pancreatic juice and of bile in the intestines is best demonstrated in the human patient by withdrawal of duodenal contents and testing these for trypsin, lipase and diastase by method of Martin (Arch. Int. Med. 1927, **39**, 343).

LIVER

Physiological and Anatomical Considerations

Concerning the function of the liver the following points may be said to have been demonstrated: 1. sugar, absorbed in the intestinal canal, is carried to the liver through the portal system, is transformed into glycogen, and is stored in the liver cells. If the sugar content of the blood falls below the normal value, or in the event of certain nervous stimuli transmitted via the N. splanchnicus, or finally, following the injection of adrenalin, the glycogen stored in the liver is broken down into glucose by means of an enzyme present in in the liver, and is discharged into the blood; 2. the liver is one, although not the only, site of the formation of urea; 3. it acts to detoxicate many toxic substances absorbed from the intestines; 4. it is a principal site of the formation of bilirubin and under normal conditions the only site of its

excretion. [**The physiology of bilirubin formation and excretion** has recently been summarized by Rich (Bull. Johns Hopkins Hosp., 1930, **47**, 338) as follows: hæmoglobin taken up from the blood stream by the phagocytic cells anchored within the capillaries of the liver, spleen and bone-marrow is split, within those cells, into bilirubin and a colorless, iron-containing residue. Both substances are then discharged into the blood stream. The bilirubin, as it passes through the capillaries of the liver, is selectively removed from the blood by the epithelial hepatic cells and is excreted into the bile canaliculi, whence it flows, mixed with the rest of the bile, through the larger bile ducts into the duodenum. Although bilirubin itself may be reabsorbed from the intestine and excreted again into the bile, most of the bilirubin reaching the intestine is reduced there to urobilin by the action of bacteria. Some of the urobilin so formed is excreted in the fæces, but some is absorbed into the blood. Under normal conditions most of the urobilin so absorbed is removed by the liver to be excreted in the bile, but under certain circumstances (e.g., with diffuse liver damage) the liver becomes unable to remove it efficiently from the blood stream and large amounts may pass from the blood into the urine.

Jaundice may therefore occur (1) if bilirubin be produced faster than the liver cells could excrete it; (2) if the excretory mechanism of the liver be so disturbed that the amount of bilirubin normally produced could not be satisfactorily removed from the blood; or (3) if there occur any combination of the above conditions. To the first type Rich applies the term "Retention jaundice"; the second he calls "Regurgitation jaundice." With his permission Rich's tables of classification are reproduced below. Ed.]

Tests of Liver Function

As the liver plays an important rôle in sugar metabolism, the following tests for ascertaining disturbance of the liver function have been drawn up.

1. Lævulose test: In the morning the patient is given 50–100 g. lævulose in a large cup of tea; during the next 6 hours the urine is collected every 2 hours. Each sample is tested with the Seliwanoff reaction (Page 219) and examined

CLASSIFICATION OF JAUNDICE
(Rich: Bull. Johns Hopkins Hospital 1930, **47** 338)

- I. RETENTION JAUNDICE
  Laboratory tests: Blood: ++ indirect v.d. Bergh
  Stools: ++ urobilin
  Urine: ++ urobilin
  Cause: Overproduction of bilirubin + subnormal liver function caused by
  - A. Anoxæmia, caused by
    - 1. Anæmia
      - Pernicious anæmia
      - Hæmolytic jaundice
      - Sickle-cell anæmia
      - Paroxysmal hæmoglobinuria
      - Mismatched transfusion
      - Phenylhydrazine poisoning
    - 2. Chronic passive congestion
      - Cardiac decompensation (especially with pulmonary infarction)
  - B. Febrile disease, associated with anoxæmia resulting from
    - 1. Anæmia
      - Hæmolytic septicæmias
      - Malaria
      - Black-water fever
    - 2. Pulmonary consolidation........Lobar pneumonia
  - C. Immaturity of liver cells in Newborn..........................Icterus neonatorum
  - D. Undetermined..Hanot's cirrhosis

- **A.** Necrosis of liver cells, caused by
  - 1. Toxic agents
    - a. Chemical
      - Chloroform
      - Carbon tetrachloride
      - Phosphorus
      - Salvarsan, etc.
    - b. Vegetable....................Mushroom poisoning
    - c. Bacterial
      - Yellow fever
      - Congenital syphilis
      - Weil's disease
    - d. Undetermined
      - 'Idiopathic' acute yellow atrophy
      - Lænnec's cirrhosis
  - 2. Severe degrees of A and B, Table 1

II. REGURGITATION JAUNDICE *Laboratory tests:* Blood: ++ direct v.d. Bergh Stools: decreased urobilin Urine: + bilirubin and bile salts *Cause:* Rupture of canalicula, caused by	B. Obstruction of bile ducts, caused by	1. Plugging	a. Calculi	Cholelithiasis Pancreatic calculi
			b. Inflammatory exudate	Cholangeitis
			c. Parasites	Fasciola hepatica Ascaris, etc.
			d. Neoplasms	Tumors of bile ducts
		2. Stricture	a. Scarring	Chronic cholangeitis Syphilitic cirrhosis
			b. Malformations	Congenital stenosis or atresia of ducts
			c. Neoplasms	Primary or secondary tumors involving bile ducts
		3. Pressure	a. Inflammatory masses in liver	Abscess Gumma Tubercle Hodgkin's disease
			b. Parasitic masses	Echinococcus cyst
			c. Vascular tumors	Aneurysm of hepatic artery
			d. Inflammatory tissue outside liver	Peritoneal adhesions
			e. Neoplasms	Tumors of pancreas, gall-bladder, liver, etc.
			f. Enlarged hepatic lymph nodes	Tumor metastases Hodgkin's disease Tuberculosis
	C. Undetermined			Catarrhal jaundice

in the polarimeter if the result is positive. The polarimeter reading is multiplied by 0.57 to calculate lævulose concentration. Excretion of over 0.7 g. signifies disease.

2. Galactose test: The patient receives 40 g. galactose in the morning on an empty stomach. The urine is collected for the next twelve hours in two-hour portions and examined for galactose by the Nylander test. If this reaction is positive the urine is examined in the polarimeter (polarimeter reading $\times$ 0.7 = g. galactose. Results over 3 g. are pathological).

Failure of retention of lævulose or galactose indicates diffuse parenchymatous disease of the liver.

Percussion and Palpation of the Liver

The upper border of the liver dulness corresponds to the lower border of the right lung and heart. The lower liver border, in the healthy individual, is between the 10th and 11th ribs in the axillary line, crosses the costal margin in the mammillary line, lies, in the midline, midway between the tip of the xiphoid process and the umbilicus and then curves upward to meet the diaphragm between the left parasternal and mammillary lines. With deep inspiration, as well as in the left lateral decubitus, the liver dulness is smaller on account of the descent of the right lung border. The lower border of the liver rises and falls slightly with in- and expiration.

In reality it is only possible, by percussion, to mark off that portion of the liver which is not overlain by lung. The uppermost border of the liver, which lies high in the thorax immediately below the dome of the right diaphragm, may be approximately localized by determination of the relative liver dulness with somewhat heavier percussion. The position of the dome of the liver and of the diaphragm may be most accurately made out by fluoroscopy. This procedure makes it possible, not only to visualize the diaphragm, but also to follow its movements with respiration. With inflammatory processes of the liver or in its neighborhood (liver abscess, subphrenic abscess, perinephric abscess) the respiratory excursions of the diaphragm are diminished or absent. The right or left half of the diaphragm may be paralyzed and assume an abnormally high position with lesions of the

phrenic nerve on the same side. This nerve arises from the 2nd to 4th cervical segment and passes downward through the thorax over the pericardium to the diaphragm.

In the normal individual the edge of the liver is either not palpable or only indefinitely so; if it be palpable one may conclude that the liver is somewhat harder than normal. An important point in palpating to determine the consistency of the liver is the sensation imparted to the finger as the liver edge passes over it, upon deep palpation: The hand is placed flat against the right upper abdomen and the finger tips are pressed inward and slightly upward as the patient inspires deeply. The patient should be examined in the horizontal dorsal position, the head must not be bent forward, and the abdominal wall must be relaxed. Caution! Palpate gently and with warm hands!

With pulmonary emphysema the liver dulness is sometimes reduced in size as the abnormally inflated lung border overrides the liver. In high grades of emphysema, due to depression of the dome of the diaphragm, the lower border of the liver may also be depressed. Such a downward displacement of the liver is also found with right-sided pleural effusion and pneumothorax.

Upward dislocation of the liver occurs with contraction of the right lung or pleura, but above all with distention of the abdomen, e.g., as a result of pregnancy, ascites, meteorism. The anterior border of the liver is thereby pressed upward so that the liver dulness is not only elevated but diminished in size.

The **gall-bladder** is usually not palpable. If, however, it be abnormally dilated it may be made out on palpation and percussion as a pear-shaped, smooth tumor in the right mammillary line just below the edge of the liver. This may be the case if it be overfilled with bile due to obstruction of the ductus choledochus, or with pus in empyema of the gall-bladder, or with a mucoid, colorless fluid in hydrops of the gall-bladder occurring with long-standing obstruction of the ductus cysticus.

Gall-stones are found chiefly in the gall-bladder but may occur in the larger bile passages. As Naunyn has shown, their formation presupposes the coincidence of stasis and

infection in the bile passages. Certain other etiological factors are, however, to be considered: Gall-stones occur more frequently in women than in men and particularly in women who have borne children; they also tend to occur in families. The gall-stones which are found in the human being are chiefly composed of cholesterin and are usually deeply stained with bilirubin. Old gall-stones, and particularly those which have lain for a long time in a chronically inflamed gall-bladder, sometimes possess a calcified shell; such stones are visible in an X-ray plate. If, however, the stones consist only of organic substances (as is usually the case) they cast no shadow in the X-ray and their presence may only be demonstrated by the method of Graham. He has shown that tetraiodophenolphthalein is excreted through the liver into the bile passages. If 3–4 gm. of this substance, dissolved in 40 c.c. of distilled water and diluted with 150 c.c. of physiological saline, be injected (sterile) intravenously in the evening, the next morning the gall-bladder (on account of its high iodine content) may be visualized by the X-ray as a circumscribed pear-shaped shadow; its emptying into the duodenum may be followed. If large gall-stones are present in the gall-bladder they produce circumscribed defects in the gall-bladder shadow. Since the infusion of such a large quantity of fluid into the vein is attended with certain difficulties the oral administration of this substance has been attempted. The absorption of this preparation from the intestine is, however, often incomplete and filling of the gall-bladder is not always possible by this method. Absorption is enhanced by the administration of a high-fat meal (cream). The presence of so large a quantity of tetraiodophenolphthalein in the stomach often leads to distressing nausea; this may be avoided by administering the drug in salol-coated capsules, which are dissolved only in the small intestine. If it may be assumed that the dye has been properly absorbed and the gall-bladder still remains unfilled it may be supposed that the cystic duct is obstructed.

X-ray examination in the human being and animal experiments, has shown that the emptying of the bile into the duodenum is the result of the stimulus of certain food stuffs, e.g. oil and the products of protein digestion; it may also be

enhanced by magnesium suphate and certain other salts. In the neighborhood of the papilla of Vater the common bile duct is surrounded by a ring of smooth muscle, the sphincter of Oddi. This is controlled by the vagus and so long as it is closed the bile from the liver passes through the hepatic and cystic duct into the gall-bladder there to undergo concentration. As the sphincter opens under the stimulus of food in the duodenum there takes place a contraction of the gall-bladder musculature with discharge of the bile from the gall-bladder.

Gall-bladder colic, characterized by attacks of terrific pain in the epigastrium, in the region of the liver, and beneath the right shoulder blade, and often by fever; the region of the gall-bladder is tender to pressure during the attack. Such attacks of gall-bladder (gall-stone) colic usually occur with inflammation of the gall-bladder or gall-duct resulting not infrequently from the inwandering of colon bacilli, typhoid bacilli, or other microörganisms. Cholecystitis and cholangitis infectiosa may lead to the formation of gall-stones, which in turn promote the infectious process. This explains the fact that in the vast majority of cases of gall-bladder colic, stones are found in the gall-bladder and the wandering or incarceration of such stones may be looked upon as the cause of the colic. Icterus is present with cholangitis and cholelithiasis whenever the ductus hepaticus or choledochus is closed by inflammation or by a stone. Jaundice is, however, often absent, and, specifically, if a stone lodges in the ductus cysticus, leaving the ductus hepaticus and ductus choledochus open. Purulent inflammation of the gall-bladder (empyema vesicæ felleæ) is a serious disease, with high and persistent fever, and striking enlargement and tenderness of the gall-bladder; operative drainage is generally necessary.

Enlargement of the liver may occur in the following conditions:

Catarrhal jaundice; the liver is usually somewhat swollen, often palpable, not tender. Spleen usually enlarged, particularly with long-standing jaundice as well as in infectious types, e.g. Weil's disease.

Liver abscess: Liver irregularly enlarged, tender, peri-

hepatic friction rub, usually icterus, irregular fever with chills. Spleen usually enlarged.

Hypertrophic cirrhosis (Hanots): Liver diffusely enlarged, with rounded edge, consistency firm. Spleen greatly enlarged, jaundice, no ascites, often a brown pigmentation of the skin, particularly that of the face.

Carcinoma of the liver: Liver shows hard nodular tumors, is usually enlarged, icterus usually present, spleen not enlarged, ascites sometimes present, cachexia.

Echinococcus disease of the liver: Liver usually irregularly enlarged with tense, sometimes fluctuating, tumors, puncture of which occasionally yields fluid from which the diagnosis may be made (complement fixation and characteristics described in chapter on parasites). Icterus sometimes present. No ascites, spleen not enlarged.

Chronic passive congestion of the liver: Present in such diseases of the heart and lungs as lead to venous congestion. Liver enlarged, firm, jaundice mild or insignificant, spleen generally not enlarged, ascites only present when accompanied by œdema of the legs and by hydrothorax.

Amyloid liver (with long-standing pyogenic disease, tuberculosis, syphilis): Liver diffusely enlarged, smooth, somewhat firm, spleen enlarged; icterus and ascites absent. Albuminuria.

Syphilis of the liver: Liver firm, either diffusely enlarged or beset with deep cicatricial furrows, spleen enlarged. Icterus and ascites sometimes present, often absent. Wassermann positive.

Leukæmia: Liver diffusely enlarged, spleen enlarged to a still greater degree, no icterus or ascites.

The **liver is diminished in size** in:

Atrophic cirrhosis of the liver (Laënnec): Liver hard, nodular, shrunken; in the early stages only the left lobe is reduced in size while the right may attain a considerable size. Spleen usually large, portal obstruction, ascites usually of a high grade, icterus insignificant or lacking, frequently profuse gastric or œsophageal hæmorrhage, urobilinuria. Between the hypertrophic and atrophic forms of cirrhosis there are many transitions. Etiology sometimes alcoholism.

Acute yellow atrophy of the liver: Sometimes following

the appearance of what is apparently the common, benign type of jaundice, delirium and somnolence ensue and the soft, and very tender liver shrinks rapidly in size. Deep jaundice, no enlargement of the spleen, no ascites. Hæmorrhage in different portions of the body. Leucine, tyrosine and other amino-acids often found in the urine.

SPLEEN

The spleen lies against the posterior wall of the abdominal cavity. Its posterior pole is adjacent to the spinal column and the left kidney. The anterior pole of the spleen normally lies in the mid-axillary line between the 9th and 11th ribs and about 3–5 cm. posterior to the costal margin. The splenic dulness is therefore to be percussed in the posterior axillary line. If the spleen undergo pathological enlargement its anterior pole is displaced forward and may be palpable as it descends with inspiration below the costal margin. It is impossible to determine by percussion either the length of the spleen or the position of the posterior pole. The height of the splenic dulness (i.e. the breadth of the spleen) in the mid-axillary line is 5–7 cm. At the end of a deep inspiration, and particularly with the patient on the right side, the splenic dulness becomes smaller on account of the depression of the left lower lung border. If that portion of the colon which overlies the spleen (splenic flexure and descending colon), be filled with fæces it may be impossible to outline it by percussion. To determine the area of splenic dulness in the presence of a full stomach it is necessary to examine the patient lying on his right side. The **splenic dulness is reduced in size** or may entirely disappear, in certain cases of emphysema in which the inflated lung border completely overlies the spleen, or with ascites or meteorism, when the spleen is pressed upward against the dome of the diaphragm.

The **spleen** may be considered to be **enlarged** if the breadth of the splenic dulness exceeds 7 cm. and the tip extends below the costal margin and is palpable. In palpating the spleen the hand is laid flat just below the left costal margin and the patient is directed to take a deep breath. It may sometimes be demonstrated that the spleen is tender, due, perhaps, to perisplenitis with resultant adhesions.

Enlargement of the spleen takes place in many infectious diseases, in typhoid (after the end of the first week of the disease) and in malaria; in addition in typhus, malta fever, trench fever, relapsing fever and in septic conditions. It is sometimes, but less frequently, enlarged in the acute exanthemata and in pneumonia at the time of, and following, the crisis. In addition, the spleen is enlarged with hepatic cirrhosis, splenic infarct or abscess, echinococcus, and malignant tumors (sarcoma) of the spleen, and amyloid disease. The greatest degree of splenic enlargement is met with in leukæmia, pseudo-leukæmia (aleukæmic leukæmia) and in Hodgkin's disease.

A syndrome consisting of primary enlargement of the spleen with secondary enlargement of the liver (cirrhosis), and anæmia, with cachexia and, in the later stages, ascites is known as **Banti's disease.** The blood picture shows diminution of the red blood corpuscles, a fall in the hæmoglobin content, and leukopænia. In **hæmolytic icterus** the spleen, and often the liver, is enlarged, and there develops jaundice, which fluctuates in severity, and in time, a severe anæmia. This disease may apparently be cured by splenectomy.

Large splenic tumors may be differentiated from other abdominal tumors in that there is usually a notch in their anterior edge and they move downward with deep inspiration. A normal spleen pushed forward by a tumor lying behind it (kidney or lymph glands) may sometimes be mistaken for a splenic tumor.

[In view of the fact that enlargement of the spleen generally leads to a tumor lying directly beneath the abdominal wall, it is often possible to distinguish between splenic tumor and tumor of the left kidney or retroperitoneal lymph glands in this region by the presence or absence of tympany upon percussion over the mass. Tumors of the kidney or retroperitoneal glands tend to push the colon in front of them, whereas the spleen, when it enlarges, usually projects in front of the colon. Ed.]

CHAPTER VII

PARASITES AND INFECTIOUS DISEASES

ANIMAL PARASITES

CESTODES (Tape-Worms)

The tape-worms represent animal colonies which consist of a head, with a prehensile organ, and a longer or shorter series of single individuals or proglottids. The eggs released from the proglottid segments develop to cysticerci in the stomach of the intermediate host and in its organs. These develop into tape-worms in the gastro-intestinal canal of the host.

Fig. 65. Segment of tænia solium.

Fig. 66. Segment of tænia saginata (after Stein).

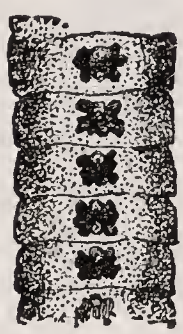


Fig. 67. Segments of bothriocephalus latus.

Fig. 68. Ovum of tænia solium.

Fig. 69. Ovum of tænia saginata.

Fig. 70. Ovum of bothriocephalus latus.

Tænia solium = pork tape-worm is 1–3 m. long. The head round, the size of a pin, with 4 suctorial discs and a rostellum upon which are arranged two circular rows of hooks. The thin cervical portion is about 1 cm. long and to this is attached the chain of segments. The mature proglottids are shaped like pumpkin seeds with genital pores arranged alternately on either side, and each contains a uterus with from 7–10 lateral branches (Fig. 65). The eggs are round (or oval), 30–35μ in diameter with a radially striated shell and an embryo with 6 hooks (Fig. 68). The cysticercus is of about the same size

and is found in pigs and human beings (in the latter when auto-infection has taken place from eggs in the stomach) beneath the skin, in the intermuscular connective tissue, in the brain, occasionally in the eye, and in other tissues. Calcified cysticerci are demonstrable beneath the skin and within the muscles by radioscopic examination.

Tænia saginata (medio-cancellata = beef tape-worm), is more common in Germany. It is thicker and longer (4–8 m.) than T. solium. Head 2 mm. broad with 4 darkly pigmented suckers lacking rostellum and hooks. The neck is only a few mm. long. Proglottids have irregularly alternating, lateral genital pores and each contains a uterus divided into 20–35 fine branches (Fig. 66). Eggs (similar to those of T. solium) oval, 40–30μ. The cysticercus is smaller and is found in beef.

Bothriocephalus latus = fish tape-worm, 5–9 m. long, head almond-shaped with 2 lateral grooves. The neck like a thread. The ripe segments are broader than their length; the uterus brown, rosette-shaped and arranged around the genital pore which opens on the flat surface (Fig. 67). The eggs oval, 50–30μ, with a brownish shell (Fig. 70). The cysticercus occurs in various fresh-water fish.

Individuals who harbor Bothriocephalus latus develop, not infrequently, changes in the blood picture very similar to those of pernicious anæmia. There is demonstrable in the body of the bothriocephalus a very toxic substance, the injection of which into animals produces either death or the picture of pernicious anæmia. A similar substance, though distinctly less toxic, is found in the bodies of other tapeworms and intestinal worms.

Tænia echinococcus = hydatid cyst. This tape-worm occurs in the dog, is only 2.5–6 mm. long, and has a head with a double row of hooks and suckers, a short neck and 3–4 segments, of which only the last one is pregnant. The cysts occur in the human being in the liver, spleen, kidneys, lungs, bones, etc. There are two forms: large **cysts,** often filled with daughter cysts, which may be as large as a child's head, and **E. multilocularis,** in which are found numbers of small, gelatine-filled cavities with concentrically laminated walls. In an echinococcus cyst heads (scolices) with hooks are some-

times found. In the blood serum of an individual harboring an echinococcus cyst specific antibodies may be demonstrated. The diagnosis may, therefore, be made by mixing the blood of a suspected case with the antigen (the sterile fluid from an echinococcus cyst), with the addition of a complement (fresh guinea-pig serum), and examining by the method for demonstrating complement-fixation described on page 328. The blood of a human being harboring an echinococcus infection contains an abnormally great proportion of eosinophilic leucocytes.

NEMATODES (Round Worms)

These worms show separate sexes.

Ascaris lumbricoides inhabits the small intestine, is usually passed in the stool, but is sometimes found in vomitus.

FIG. 71. Ovum of Ascaris lumbricoides.

FIG. 72. Ovum of oxyuris vermicularis.

FIG. 73. Ovum of Trichocephalus dispar.

FIG. 74.

FIG. 75.

Ova of ankylostoma duodenale.

In the ascaris organism there are formed a variety of substances which are pharmacologically active and which may produce a variety of symptoms. A massive accumulation of ascarides may, in rare cases, lead to intestinal obstruction. Ascaris is similar to the earth worm; the male is somewhat smaller (15–20 cm.) than the female (25-40 cm.) and the head is often involuted. The eggs, which are often passed in quantities in the stool, are oval, 70–40μ and have a thick, concentrically striated shell, without which there lies a protein hull covered with small knobs (Fig. 71).

Oxyuris vermicularis, the pin-worm, infests both small and large intestine and even the vermiform appendix, may sometimes leave the intestine and produce a superficial inflammation in and about the anus. It is a thread-like little

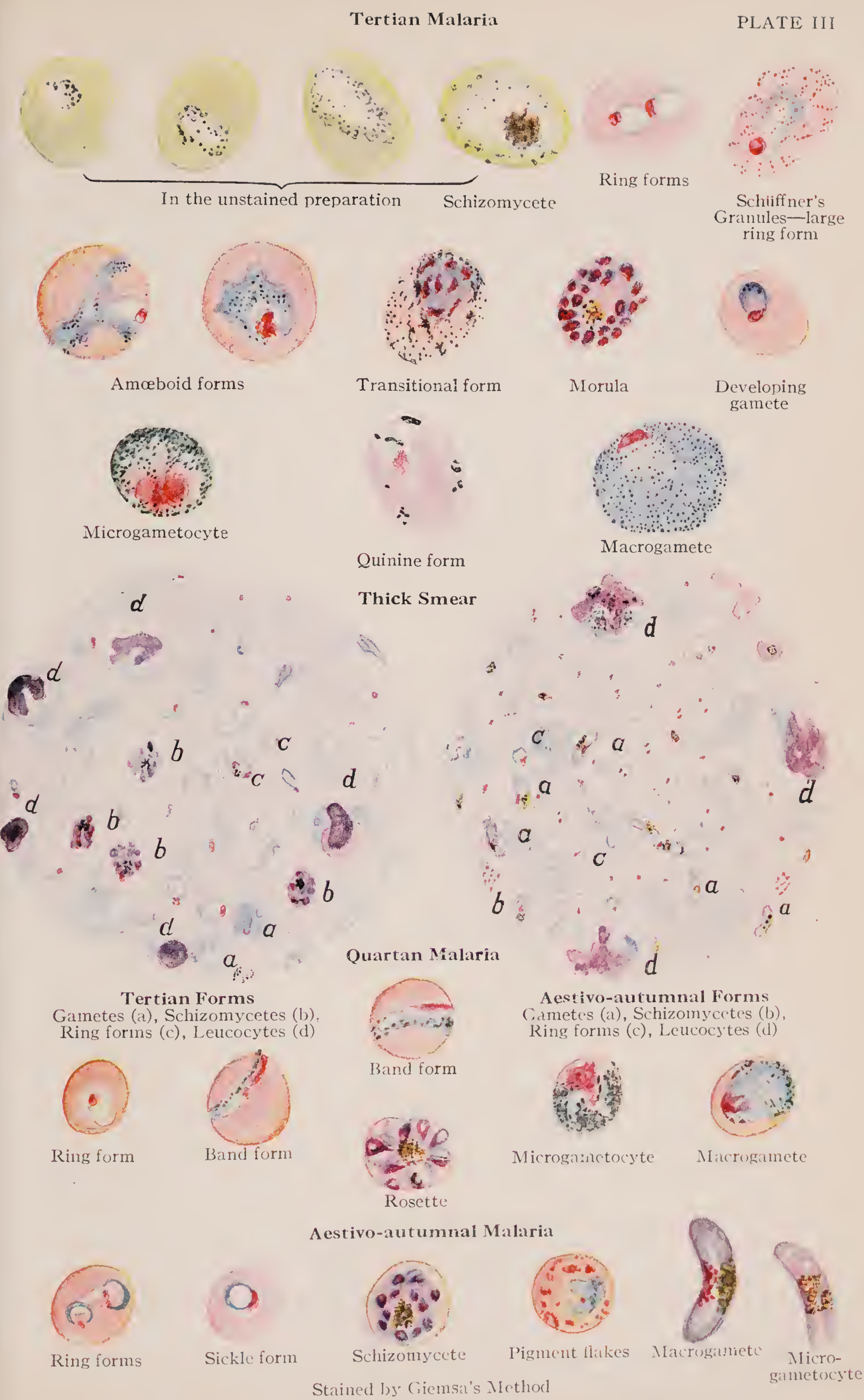
worm, the male 3–5 mm., the female 10-12 mm. in length, the former with a short and involuted caudal end, and the latter with a long, pointed tail. The eggs, which are often found in the softened skin about the anus of the patient, are irregularly oval in shape with a thin shell 50–20μ in size (Fig. 72). Infection most often from soiled fingers; auto-infection, in the same fashion. Patient should be warned against scratching the perineum with the fingers.

Trichocephalus dispar (Trichiuris trichiura), whip-worm, is 4–5 mm. long; has a thread-like head and a thick body, involuted in the male, and in the female straight or slightly bent. Eggs yellowish-brown, 55–20μ, the form of a lemon with a knob-like protrusion at both poles (Fig. 73). Infection by dirty hands and fingers (drinking water?).

Anguillula intestinalis (Strongyloides stercoralis), 1.8–2.3 mm. long, infests the upper portion of the small intestine. The eggs, which are similar to those of Ankylostoma duodenale, are passed containing completely developed embryos. These break through the shell and appear in the fæces as small embryos (0.2–0.3 mm. in length), which rapidly develop into motile worms.

Ankylostoma duodenale, hook-worm—male 10 mm., female 12–13 mm. long, inhabits the small intestine of the human being and produces its action by boring through the intestinal wall and absorbing its blood supply, and by the elaboration of a poisonous substance which produces a severe anæmia (tropical chlorosis, anæmia in the laborers in the St. Gotthard tunnel, and brick-makers anæmia). The oval (60–35μ) eggs, which are passed in quantity in the stool, have a hard shell and contain the embryo (Figs. 74–75). These embryos develop within the shell after they have been voided, break out, develop and begin within the next few days to desquamate. The larvæ may gain entrance to the gastro-intestinal canal of the human by penetrating the skin and entering the blood stream; they are then carried to the lungs, are coughed up and then swallowed into the intestine where they develop into mature sexual forms.

Trichina (Trichinella) spiralis. The normal host is the rat, from which the pig is infected. If pork containing trichinæ be taken into the human stomach the capsules of the muscle


Tertian Malaria
In the unstained preparation
Schizomycete
Ring forms
Schüffner's Granules—large ring form
Amœboid forms
Transitional form
Morula
Developing gamete
Microgametocyte
Quinine form
Macrogamete
Thick Smear
d
d
b
c
c
d
d
b
b
b
d
a
a
d
c
a
a
a
c
b
a
a
d
d
Quartan Malaria
Tertian Forms
Gametes (a), Schizomycetes (b), Ring forms (c), Leucocytes (d)
Band form
Aestivo-autumnal Forms
Gametes (a), Schizomycetes (b), Ring forms (c), Leucocytes (d)
Ring form
Band form
Rosette
Microgametocyte
Macrogamete
Aestivo-autumnal Malaria
Ring forms
Sickle form
Schizomycete
Pigment flakes
Macrogamete
Micro-gametocyte
Stained by Giemsa's Method

trichinæ are dissolved and the parasites are freed and develop in the intestine into mature trichinæ (male 1.5, female 2–4 mm. in length). The female buries itself in the intestinal wall, where, after 5-7 days, she deposits young living trichinæ; these reach the blood stream by way of the lymph vessels and, in the course of the next day or two, are deposited in the muscle fibers, where, after several weeks, they become encapsulated. Encapsulated trichinæ may be demonstrated in the musculature by means of X-ray. The presence of trichinæ in the intestine gives rise to severe gastro-enteritis, and their deposit in the muscles leads to fever and myalgia. In the differential diagnosis, as contrasted with other infectious diseases, it is of importance that in trichinosis there is a conspicuous eosinophilia, that the urine gives a strong diazo-reaction, that the knee-jerks are sometimes absent, and that, not infrequently, the eyelids are swollen. Trichinæ embryos are almost never found in the stool but may sometimes be isolated from the spinal fluid. Concerning the demonstration of the embryos in the blood see page 181.

Filaria sanguinis (F. Bancrofti), occurs principally in the tropics and is carried to the human being by the mosquito. It causes hæmaturia, chyluria and disturbances in the lymph circulation (elephantiasis). The mature forms infest the lymphatic organs of the human being and set free living embryos in large numbers. These may be present in the urinary sediment or in the blood, in the latter often in so great numbers that each drop of blood may contain several. They appear as actively motile little snakes surrounded by a tough shell, about 0.216 mm. in length and of the diameter of a red blood cell.

TREMATODES (Flat-Worms)

Distomum hepaticum (Fasciola hepatica), liver fluke; 20–30 mm. long, shaped like a leaf with a cone-shaped prolongation at the anterior end and two suckers on the surface near the head. The eggs are very large, 0.13 mm. in length (Fig. 76) and eliptoid.

Distomum lanceolatum (Opisthorchis felineus) is smaller than the above, about 11 mm. in length, lancet-shaped. The eggs are also considerably smaller. Both forms infest the gall

passages producing dilatation and inflammation of the bile ducts with inflammation and subsequent atrophy of the liver. The eggs are sometimes found in the fæces.

Distomum hæmatobium (Bilharzia) occurs in the tropics, infests the portal vein and its radicals and the vessels of the urinary bladder, causing diarrhœa, hæmaturia and chyluria (Bilharziosis). Male 12–14 mm. long, female up to 20 mm. in length. The eggs, 0.12 mm. long, appear in the urinary sediment and show a point either at one pole or on one side, (Fig. 77) 120 μ long, 50 μ wide.

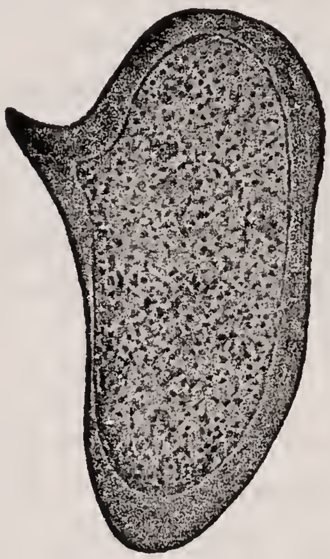


Fig. 76.
Ovum of distomum hepaticum.

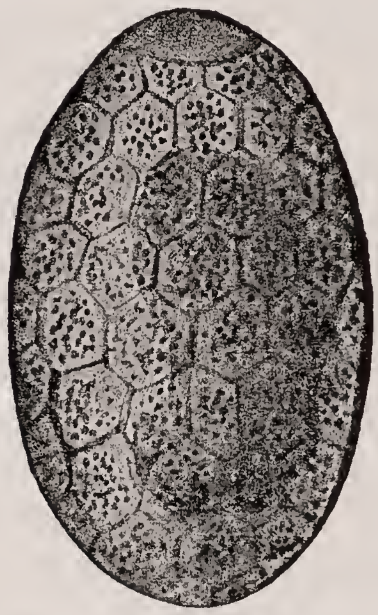


Fig. 77.
Ovum of distomum hæmatobium.

Distomum pulmonale, 8–10 mm. long, 4–6 mm. wide and shaped like a plump egg. Color like that of the earth worm; mouth and abdominal suckers of equal size. Eggs, found in large numbers in the bloody fæces, of a brownish-yellow color, 0.08–0.1 mm. long and 0.05 mm. wide with a cap on the blunt end. They occur in cavities in the periphery of the lungs and cause a persistent cough with the expectoration of a dirty brownish-red sputum.

ARTHROPODS

Mites, ixodidæ, the larvæ from various species of mites which live in shrubs and grass, sometimes enter the exposed skin, e.g., over the legs, and cause pruritis, erythema, eczema or urticaria. The blood-sucking parasite is to be identified macroscopically in the cutaneous lesion. **Leptus**

autumnalis (harvest bug) a red colored mite visible to the naked eye, may invade human beings in autumn from gooseberry bushes. **Ixodus reduvius,** wood tick, dog tick (ixode), 1–4 mm. long, may bore deep into the skin, leaving only a small mark. If, however, the insect is carelessly removed the head frequently remains in the wound and causes an inflammatory reaction. **Ornithodorus moubata** which lives in the soil of native huts of certain regions of Africa and invades the naked limbs of the inhabitants transmits the spirochæte Duttoni, the cause of African relapsing fever.

~~**Acarus**~~ (sarcoptes) scabiei, itch mite; has an eliptoid body shaped like a turtle, with 8 short legs. The female lies at the end of a burrow in the epidermis which is filled with eggs and particles of fæces. After 8–14 days the young are hatched and penetrate the skin.

Three types of **lice** infest the human being: (1). the **head louse, pediculus capitis,** which lays its eggs, the so-called "nits," upon the hairs. (2). The **crab louse, pediculus pubis,** having a roundish body; the "nits" are found in the pubic hair and also in that of the axillæ. In the presence of crab lice faint blue flecks the size of a bean, maculæ cœruleæ, are found upon the skin of the infested individual. (3). The **body louse, pediculus vestimentorum,** lays its eggs upon the clothes but sometimes upon the human hair, and for these reasons, to destroy all parasites, it is necessary to delouse the clothes and the beds.

Lice are blood-sucking parasites and they may transmit infection by their bites. The body louse carries typhus exanthematicus, five-day fever, and relapsing fever. In the intestine of the body louse which has sucked blood from a patient with typhus fever, Rickettsia may be demonstrated (see page 370).

Various bugs, ticks, and fleas may transmit infectious diseases by their bites, obtaining the organism from the blood of one individual and transmitting it to another, e.g. relapsing fever and the plague. In the dispersion of the latter the fleas of dogs and rats are also implicated.

PROTOZOA

Amœbæ are sometimes present in the stool. They are round or ovoid bodies slightly larger than a white blood cor-

puscle; they possess a round nucleus with a nucleolus and their cytoplasm is finely granular. If observed immediately following evacuation either in a **warm chamber** or upon a warm slide they may be seen to be **motile,** throwing out pseudopodia, which contain only glistening and entirely structureless material. Amœbæ are occasionally found in the stools of healthy individuals and rather more frequently in association with chronic diarrhœa (entamœbæ coli). Entamœba histolytica (Shaudinn) is a pathogenic form, the cause of amœbic dysentery. This disease is more common in the tropics and is characterized by severe inflammation and ulceration in the colon, with fever and bloody, mucoid diarrhœa. It is prone to relapse, and, in contrast to the bacillary form, is frequently complicated by abscess of the liver. The bloody mucoid stools of amœbic dysentery contain relatively few leucocytes, in contrast with those of bacillary dysentery in which leucocytes are present in abundance. Entamœba histolytica buries itself in the mucosa and submucosa of the gut causing destruction of tissue and inflammation. The transfer, by means of a swab, of a small amount of fæcal material containing amœbæ from such a case into the upper rectum of the cat produces the characteristic disease and ulceration in the intestine of this animal.

Entamœba histolytica is round or oval; sharply marked off from the glandular endoplasm is the highly refractile ectoplasm which is thrown out in sacular protrusions to engulf nutrient material (bacteria, red and white blood corpuscles). The endoplasm is of a web-like structure and contains, in addition to a vacuole and a round nucleus, a large number of droplets and inclusions, e.g., blood cells. Multiplication is by simple fission. As the dysentery heals and conditions become less favorable for the nutrition of the amœbæ smaller forms appear, which do not penetrate the intestinal mucosa but multiply rapidly in the intestinal contents. From these forms cysts develop which are enclosed by a membrane and possess at first two and later four nuclei. It is probable that these cysts, contaminating drinking water, serve to infect otherwise healthy individuals. In addition to the entamœba histolytica another form (**entamœba tetragena**) is described as causing tropical diarrhœa, but it is highly

probable that this amœba is identical with entamœba histolytica. Amœba may be stained by the method of Giemsa: Fix with methyl alcohol, treat with 1% tincture of iodine for 5 minutes, wash in water, drain, 1½ minutes in Lœffler's methylene blue, wash in water, drain, 1 minute in concentrated eosin solution (diluted 1 : 3 with water), wash and dry with filter paper. The result is a contrasting stain of red and blue.

Trichomonas intestinalis, ciliated, almond-shaped, 10–15 μ long. Trichomonas appears in the stool and sometimes in

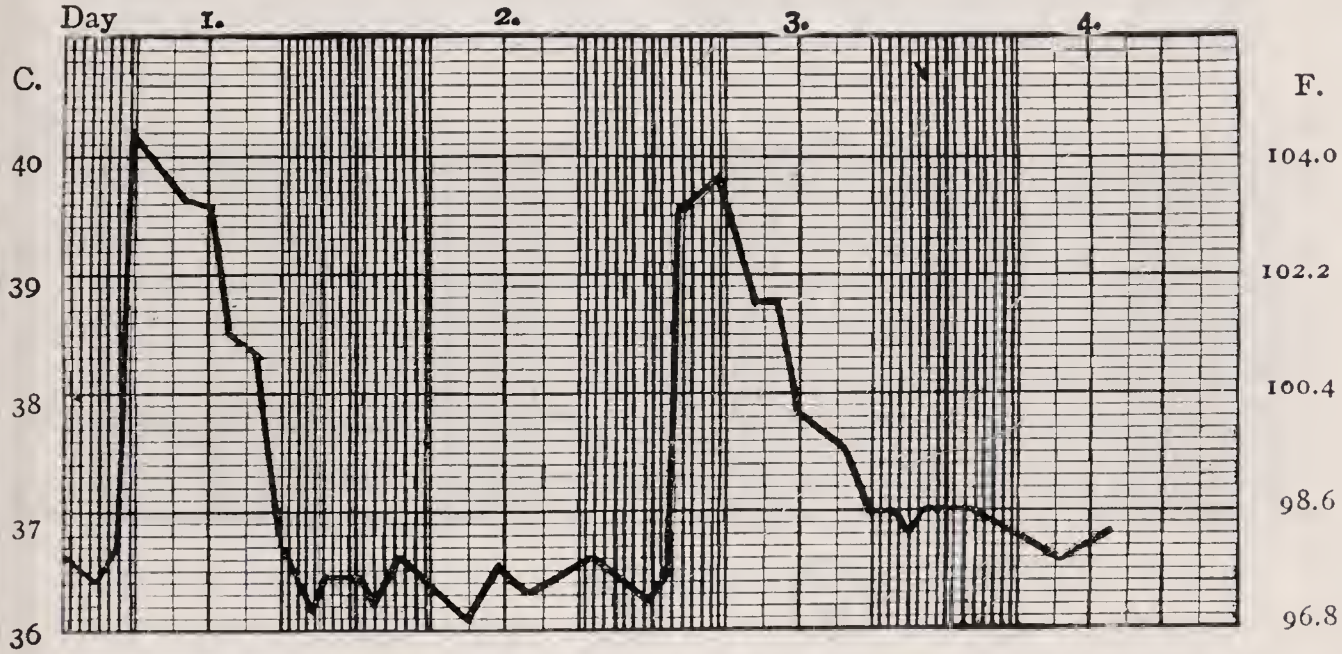


FIG. 78.—Tertian malaria. Developmental stages of tertian plasmodium.

putrefied gastric contents. **Balantidium** or **paramæcium coli,** egg-shaped, 7–10 μ long, ciliated with an invaginated mouth orifice. **Megastoma entericum** (Lamblia intestinalis) pear-shaped, 15.5–16.6 μ long, 10–12.5 μ wide. Protozoa are best demonstrated by shaking the freshly obtained gastric contents with water.

MALARIAL PARASITES

In malaria there are present in the blood small parasites (plasmodia), which penetrate the red blood corpuscles. They appear at first within the red cells as small, brightly staining masses which are actively amœboid. The early

stages of the vegetative form of this plasmodium possess a vacuole which fails to take up the dye; these forms appear as rings in the stained preparation. Upon the thinner portion of the ring, as stained blue by Giemsa's method, there lies a bright red mass of chromatin. As the plasmodium develops it loses the vacuole, absorbs the hæmoglobin from the red cell in which it is contained, and deposits a pigment (malaria-melanin) formed from this hæmoglobin. The plasmodium becomes so large within two or three days as almost completely to fill the red blood corpuscle. Then commences the asexual division, **schizogony.** The pigment, which formerly was arranged about the periphery, collects in the center, the

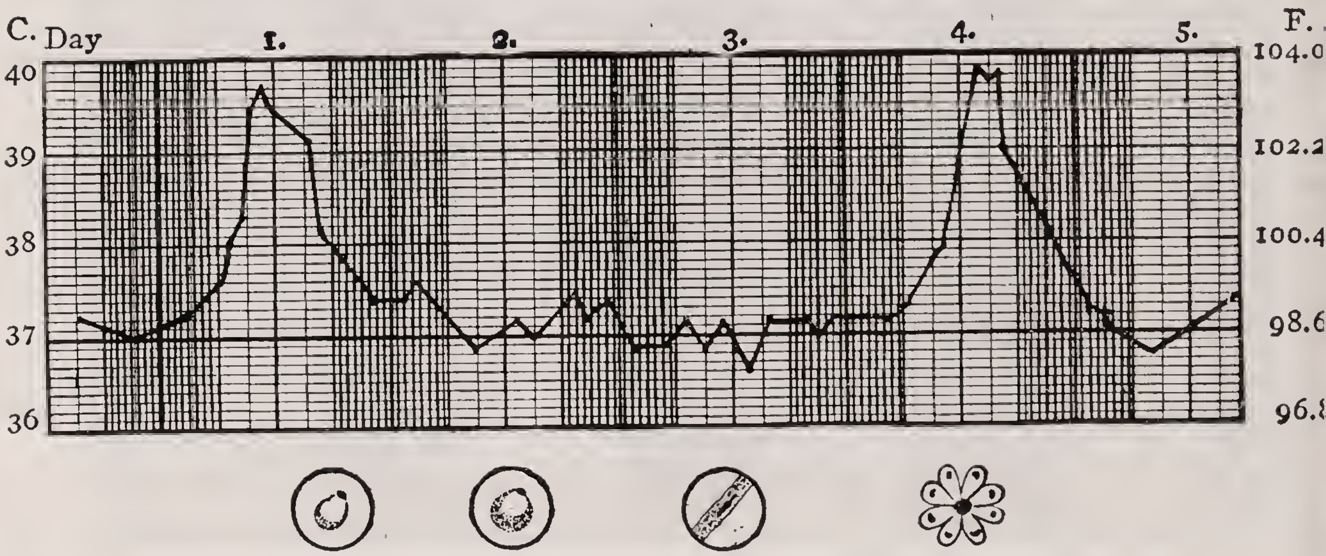


FIG. 79.—Quartan malaria. Developmental stages of quartan plasmodium.

chromatin divides, the plasmodium assumes the form of a mulberry or rosette (Morula), and splits into from 6–24 daughter organisms, the so-called **merozoites.** As the morula breaks up, these segments are thrown into the blood stream, where they penetrate other red blood corpuscles and, within them, undergo the same development cycle. With characteristic intermittent fever, in which the febrile attacks follow at regular intervals interspersed by afebrile periods, all the plasmodia present in the blood mature and divide at the same hour, and their discharge into the blood stream is accompanied by the characteristic chill.

In addition to this **asexual** type of reproduction there occurs also a **sexual** form: Single merozoites develop into larger female macrogametes and others into smaller male microgametocytes. From the latter are formed 4–8 flagellated,

spermatozoa-like strands of protoplasm, the microgametes. The copulation of this male sexual form with the female macrogamete does not take place in the human blood but in the body of certain species of mosquito, anopheles, after the mosquito has withdrawn blood from a patient infected with malaria.

This type of mosquito represents the intermediate host of the malaria parasite. Malaria as a disease is, therefore, most common in swampy districts infested by the anopheles. These are distributed all through Central Europe and in hordes in the lower Danube valley, in Roumania, in the Balkans (Macedonia) and in Italy. However the anopheles carries the malarial parasite only when an opportunity has been afforded for it to obtain this parasite from the blood of a malarial patient.

Following the copulation of the macrogametes and the microgametes in the stomach of the mosquito the parasite develops into a spindle-shaped form which burrows into the stomach wall and, beneath its epithelium, develops into the oöcyst. The numerous daughter nuclei of these oöcysts (sporoblasts) divide into enormous numbers of fine filamentous (sporozoites). These break through into the cœlom of the mosquito and are carried to the salivary glands whence they are introduced into the blood stream of the human being with the bite of the mosquito. Penetrating the human red blood corpuscle the parasites develop as described above. The first febrile attack usually takes place 11 or 12 days following the infecting bite of the anopheles.

Three forms of malaria are to be distinguished, corresponding to three types of the parasite. In **tertian malaria** the febrile attacks are repeated every 3rd day, due to the fact that the developmental cycle of the plasmodium lasts almost exactly 48 hours. In case two generations of parasites are introduced into the blood of the same individual they may produce daily febrile attacks provided that their developmental cycles proceed alternately to maturity (quotidian fever). The plasmodium of tertian malaria is identified by its particularly active amœboid movement and is, therefore, named **plasmodium vivax.** The merozoites first form rings which grow into peculiarly shaped clumps. At the same

time the blood corpuscle in which the parasite is contained undergoes a conspicuous enlargement and, upon staining with Giemsa's method, there are apparent in the protoplasm of the blood corpuscle a number of red-staining granules (**Schueffner's granules**). These two characteristics make possible the differentiation of the tertian form from that of the quartan and æstivo-autumnal. Upon division the tertian rosette form breaks down into 15–25 merozoites.

The developmental cycle of the **quartan** parasite proceeds somewhat more slowly, lasting about 72 hours; the febrile attacks take place, therefore, every 4th day. Double infection may also take place in this form (febris duplicata). The plasmodium of quartan malaria (**plasmodium malariæ**) shows at first the same ring forms as plasmodium vivax, but these are soon stretched to thin bands which gradually thicken, and lie diagonally across the red blood cell. In contrast to the tertian, the red blood corpuscle infested with the quartan parasite does not become enlarged. The pigment is darker in color and more coarsely layered. The quartan rosette is composed of from 8–12 merozoites.

The sexual forms (gametes) of tertian and quartan show great similarity; they are to be distinguished by the absence of vacuoles which are characteristic of the asexual plasmodia. The female macrogametes are rather large, solid clumps with deep blue protoplasm and compact fine chromatin in the stained preparation; the male microgametocytes are smaller and their nuclear substance, from which the microgametes develop, is more loosely distributed. Sexual forms tend to appear only after the patient has carried the malaria for a considerable time; they are more resistant to quinine (not, however, to plasmochin) and tend to accumulate in the spleen. After a considerable interval merozoites may develop from these forms by parthenogenesis. In this way the relapses of malaria are brought about.

The far more malignant form, **æstivo-autumnal malaria** of the Italians (malaria tropica) prevails in the Mediterranean countries and in Africa. Febrile attacks at regular intervals are rare except early in the disease; sometimes after an irregular course the fever may be almost continuous and coma may ensue. The development and division of all the

parasites in the infected blood does not take place at the same time and as a result various stages of development are to be found in any given specimen. The plasmodia of tropical malaria are small and highly refractile, and often several are to be found in a single corpuscle. Upon staining with Giemsa's method, the plasmodia appear as small, blue seal rings with brightly staining red nuclei, similar to the early forms of tertian and quartan, but usually smaller than the latter and often with widely distributed chromatin. The plasmodia of this form are less frequently met with in the circulating blood and are usually absent from it during a febrile attack; they tend to accumulate more in and about the blood vessels of the internal organs, e.g., the capillaries of the brain and spleen, and here the segmenting forms are found almost exclusively. The sexual forms of malaria tropica are crescent-shaped (as described by Laveran) and are not infrequently found in the circulating blood; these are typical of æstivo-autumnal malaria. In the more severe forms of malaria following the use of quinine there may appear high fever and severe hæmoglobinuria, so-called **black-water fever.**

In all forms of malaria the spleen is enlarged, often conspicuously so. In the blood of malarial patients and particularly in chronic cases the large mononuclear cells are increased in number. This may be of diagnostic significance in doubtful cases. Moreover, malaria is only to be considered cured when neither the parasites nor this mononucleosis is found in the blood. In typical febrile attacks and especially those of tertian and quartan the temperature rises slightly just before the beginning of the chill and then climbs rapidly to 39.5–41° C. (103–106° F.). The peak is generally passed within an hour or two thereafter and during the subsequent diaphoresis the body temperature sinks to normal or even sub-normal.

In some stages of the attacks (not in latent stages) the Wassermann reaction is positive in about 1/3 of all cases.

The severe, so-called pernicious, forms of the disease develop as serious infections with high grade anæmia or with dangerous localization of the causative agent (meningitic, pneumonic, dysenteric forms).

In small children the disease picture is usually atypical;

instead of rigor, convulsions frequently occur so that the infection may be overlooked.

Malaria inoculata, induced by injection of human blood containing plasmodia in the treatment of syphilis of the central nervous system, often lacks certain characteristics of the acquired disease.

Malaria inoculata ordinarily pursues a much milder course than the "natural" disease and is distinguished by the irregularity or frequency of the febrile attacks. As a result of repeated transfer from man to man the plasmodium apparently undergoes attenuation. Examination of the blood of a patient with malaria inoculata may reveal plasmodia in several stages of development in the same smear. Maturing at different times some parasites may invade the blood one day and some the next; pure "tertian" fever is thus seldom seen. The patient may have daily chills, rigor on alternate days or, rarely, two febrile attacks on the same day. Of particular advantage to the use of malaria inoculata in the treatment of syphilis is the unusual sensitivity of the plasmodia to quinine under these circumstances. Thus it is usually possible to interrupt the malaria promptly whenever desired.

The malarial plasmodia may be demonstrated in the unstained specimen by examining a drop of fresh blood under the immersion lens; under these conditions they appear as small mobile clumps of protoplasm containing moving pigment granules. The stained preparation is made from a dried smear fixed in methyl alcohol. Staining is carried out as described by Giemsa (page 163).

When the malarial parasites are scarce in the blood the **thick drop preparation** is useful: Place a large drop of blood upon a slide and allow to dry in the air. Add aqueous Giemsa's solution, allow to stand for 15 minutes, rinse with water and dry in the air. Examine with oil immersion lens. Or place the preparation for several minutes each in an atmosphere of 2% formalin and ½–1% acetic acid solution to remove the hæmoglobin. After drying stain by Giemsa's method. In the middle figure of the accompanying plate, ring and crescent forms of the æstivo-autumnal types are illustrated. In latent malaria the plasmodium may be caused to enter the blood stream by a variety of "provocative" measures, e.g., cold bath, exercise, massage of the spleen or injection of adrenalin.

TRYPANOSOMA GAMBIENSE

The cause of the **Sleeping Sickness,** widely prevalent in Africa, is a small fish-like flagellate, which is actively motile in the blood plasma; it possesses an undulating membrane, and is about 2–3 times as long as the diameter of a red blood cell (Fig. 80). It is demonstrable in the juice obtained by puncture from enlarged cervical glands and occasionally in the blood or spinal fluid. Examination of the fresh blood in a dark field is particularly adapted to the demonstration of the parasites. All observations should be controlled by Giemsa's stain. After chronic enlargement of the lymph glands, the disease passes over into a febrile state of semi-coma with symptoms of organic disease of the brain and spinal cord, and may lead to death. It is transmitted by a biting fly,

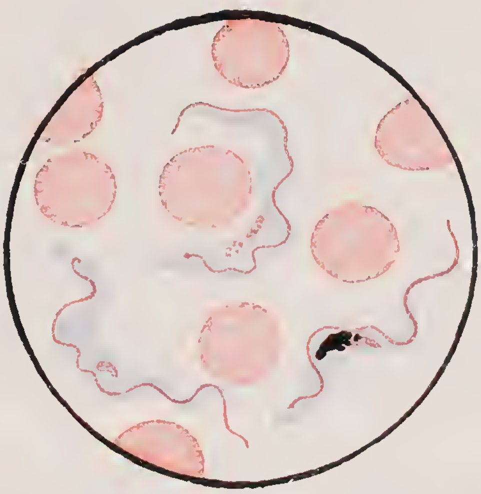


FIG. 80.—Trypanosoma Gambiense. Blood.

Glossina palpalis, which is infected by biting another patient suffering from sleeping sickness. Other trypanosome diseases occur in cattle, horses and mules; e.g., nagana, which is widely prevalent in South Africa, is caused by **Trypanosoma Brucei** and is transmitted by the **Tsetse fly.**

To the human diseases due to trypanosoma belongs Chagres fever, caused by Schizotrypanum Cruci, which is transmitted by a species of bug. In endemically infected regions the entire population is stricken by this disease. The acute disease is manifested usually in children during the first year of life. Its characteristics are enlargement of the thyroid with myxœdema and enlargement of the lymph glands, spleen and liver.

Kala-azar or **tropical splenomegaly** is a disease of the tropics characterized by irregular fever, great weakness and anæmia, gastro-intestinal disturbance and, usually, conspicuous enlargement of the liver and spleen; it is often fatal. In the liver and spleen, and sometimes in other organs, as well as in the blood, are found **small round bodies** having a large nucleus and an accessory nucleus described by **Leishman and Donovan.** In blood-containing media these bodies develop into flagellates very similar to trypanosomes. Transmission probably by blood-sucking insects.

Oriental boil produces furuncle-like abscesses upon the uncovered portions of the skin. In these lesions are found

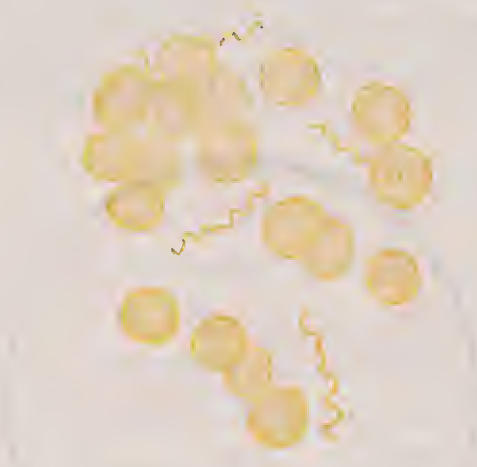


Fig. 81.—Recurrens spirochætæ in fresh, unstained blood preparation.

binucleate, round parasites which are extraordinarily similar to the Leishman-Donovan bodies of kala-azar.

SPIROCHÆTÆ

The spirochætæ of **relapsing fever (recurrens of Obermeier)** (Fig. 81), gracile, actively motile, corkscrew forms are present in the blood only during the febrile phases of this disease. They are demonstrable in an unstained droplet of blood under a magnification of about 350 diameters and are recognized by the fact that, by virtue of their motility, they collide with the red blood cells and cause them to move. They are also to be demonstrated in a stained smear fixed with aqueous fuchsin solution and stained by Giemsa's method. The thick drop preparation, as described for the demonstration of malarial plasmodia, is also useful. The injection of spirochætæ-containing blood into human beings

and monkeys produces the typical disease. Robert Koch was able to prove that the organisms of African relapsing fever were carried by **ticks** (Ornithodorus moubata), which abounded in the huts of the aborigines, and were deposited by these insects in the human beings. In addition to these ticks, lice (particularly the body louse) and fleas play a part in the transmission of relapsing fever from patient to patient. The spirochætæ are demonstrable in the intestinal contents of the body louse. Those of the African, Indian and American relapsing fever are distinguishable from the European form not so much by their morphology as by their immunological and biological characteristics.

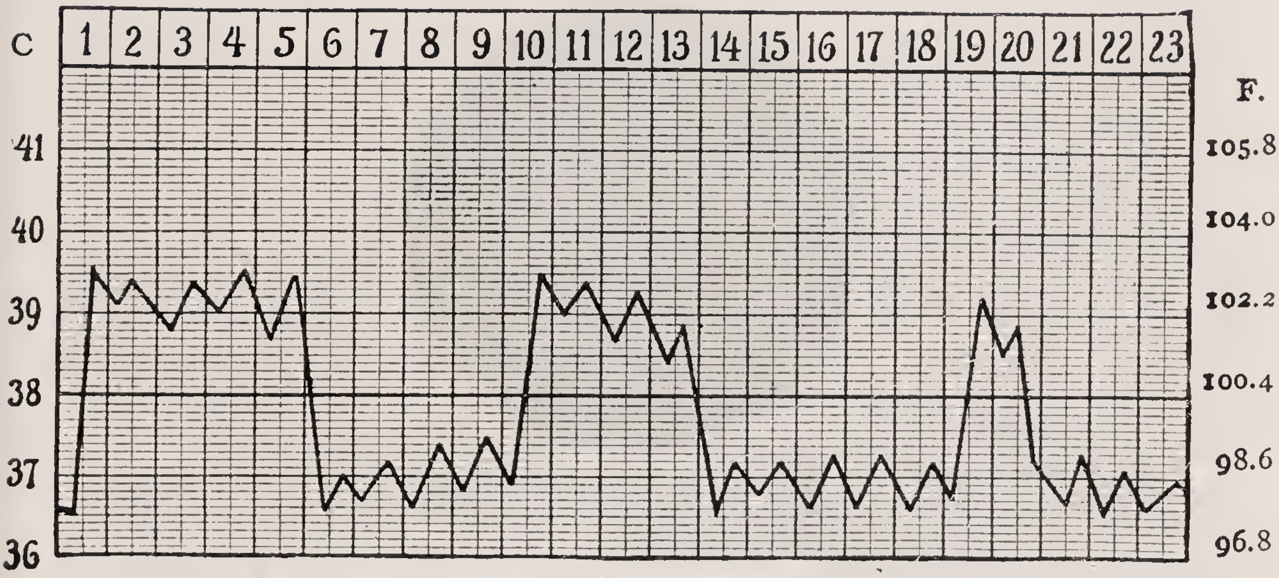


Fig. 82.—Relapsing fever.

The incubation period lasts from 2–14 days. Prodromal symptoms are not pronounced. The fever begins with a violent chill; the temperature rises rapidly, remains high for from 5–6 days, and then falls critically with sweating, and often diarrhœa. After an afebrile period of about a week a second bout of fever begins in a similar fashion but lasts a shorter time. Often a third attack, lasting only 24–48 hours (Fig. 82) occurs after an interval of 5-7 days. During the febrile stages there are severe constitutional symptoms with pain in the head, back and particularly in the calf of the leg. Stupor, spleen enlarged and tender, sometimes herpes, light jaundice and often generalized œdema. In the afebrile periods there is a striking bradycardia. The most severe forms show deep icterus, enlargement of the liver, profuse, and often bloody, diarrhœa, delirium or coma. Recently the artificial infection with these spirochætæ (mouse blood) has been employed in the treatment of general paresis (Plaut).

Spirochæta pallida (Schaudinn-Hoffmann) (Fig. 83), an extremely delicate and gracile motile spirochæta carrying a fine flagellum at either end. These are found in all stages of syphilis, in the primary lesion, in the diffuse secondary eruptions, in the bone marrow, in the vessel walls and adrenals, and scattered throughout the organs in congenitally syphilitic infants. They are sometimes found in the brain of the paretic but only rarely in the blood and in the urine (with syphilis of the kidney). They may be demonstrated as follows: The primary lesion or an open papule is vigorously rubbed with a sterile sponge and the serum which exudes is collected upon a slide; or the chancre may be scraped with a spatula and the

FIG. 83.—Smear of serum from primary syphilitic lesion—Dark-field illumination.

scrapings examined. For staining see the method of Giemsa as described on page 163. By this method the spirochæta pallida is stained pale bluish-violet while the other, coarser types of spirochætæ, e.g., spirochæta refringens, are more deeply colored. Under the dark field the spirochætæ appear as refractile and highly motile, spiral forms. **Burri's method:** A drop of serum may be diluted with distilled water, and a drop of india ink may be added and thoroughly mixed. The mixture is then streaked upon a slide and examined. Here the spirochætæ are light against the dark background. For the demonstration of spirochætæ in sections of tissue the silver-impregnation method of Levaditi is used. Noguchi has succeeded in cultivating the spirochæta pallida outside the body. A transfer of these to monkeys, rabbits and mice produces syphilis in these animals. Concerning the diagnosis of syphilis by the Wassermann reaction see page 329.

Weil's disease, an infectious jaundice associated with fever, enlargement of the spleen, hæmorrhages in the skin and mucous membranes, and often albuminuria, has been demonstrated by Inada, Heubner and Reiter, Uhlenhuth and Fromme to be transmissible to guinea-pigs by inoculating with the blood of a patient. In the blood and the liver of the affected guinea-pig, small organisms are found similar to spirochætæ but less crooked; these are regarded as the causative agent of Weil's disease (**Spirochætæ icterohæmorrhagiæ**). These spirochætæ may be cultivated in serum or blood-containing media. To establish the diagnosis about 2 c.c. of blood should be withdrawn from the patient and injected into the peritoneum or, better, into the heart of a guinea-pig. The animal dies and the autopsy findings are similar to those of the human disease. Such transmission of the disease is only possible during its early stages. In the serum of the convalescent protective bodies are demonstrable. In the later stage of the disease the spirochætæ tend to lodge in the kidney and, after the 10th day, may be demonstrated in the urinary sediment.

THE INVISIBLE DISEASE-PRODUCING AGENTS

In a number of infectious diseases the mode of transmission is understood but the causative agents have not been identified. These causative agents are apparently so small that they cannot be seen microscopically. By reason of their ability to pass through the finest pores of a filter-candle of burnt but unglazed clay this group of organisms is known as "filter-passers." The filtrate from this clay filter-candle proves to be infectious upon transmission to certain animals as well as to human beings; upon transfer to certain media, containing bits of living tissue, the organisms maintain their pathogenicity; moreover they appear to multiply in culture.

To this class of "filtrable viruses" belong the causative agents of measles, chicken pox, small pox, and probably also yellow fever, five-day fever, rabies, Pappataci fever, dengue fever, poliomyelitis, hoof-and-mouth disease, molluscum contagiosum and the common cold. The mode of infection and the symptoms of these diseases are described below. Finally, it has also been demonstrated that the causative

agent of certain malignant tumors occurring in animals, e.g., Rous-sarcoma, can pass through the clay filter-candle. The inoculation of rabbits with the contents of herpes vesicles may induce a form of encephalitis due, supposedly, to the Herpes virus. To the filter passers also belong the Bacteriophages which are responsible for the phenomenon of d'Herelles.

VEGETABLE PARASITES

HYPHOMYCETÆ

This class includes a number of vegetable parasites some of which are pathogenic and some simply saprophytic upon

Fig. 84.—Trichophyton tonsurans.

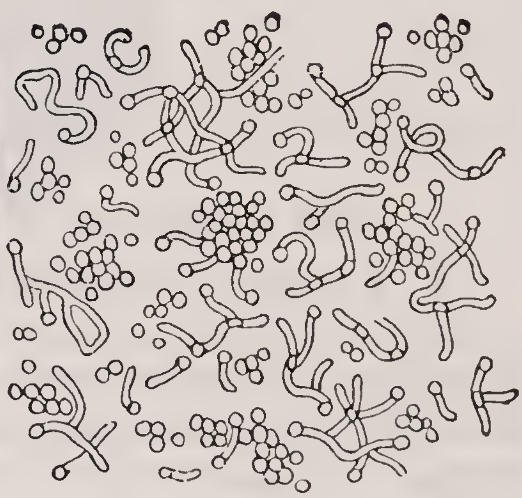


Fig. 85.—Microsporon furfur.

the skin and mucous membrane. These fungi have not been sufficiently studied for their accurate botanical differentiation. The hyphomycetæ fibers are double contoured, are branched and divided by septa. The terminal segments bear either round spore-bearing capsules, or a row of spores: highly refractile, rounded bodies of a diameter somewhat greater than the filament. In certain other forms, Oidii, the fibers themselves break up into a number of round or oval spores.

Culture, which is indispensable to the accurate differentiation of the various forms, is best carried out on peptone agar (1.5%) or maltose agar (4%) at room temperature.

The more important types are: **Achorion Schœnleinii**—the **favus fungus.** This forms yellow lesions upon and in the scalp consisting of compact, twisted fibers which are branched and divided by septa, and of round conidii. Such lesions upon the skin interfere with the growth of hair and produce scar formation.

Trichophyton (**Sporotrichum** of the botanists) (Fig. 84). A variety of forms of this type produce herpes tonsurans (Trichophytia superficialis) on the scalp and skin. If they are more virulent and bury deeper into the skin (Trichophytia profunda) they produce tinea sycosis, ring-worm, or acne mentagra, with swelling and sometimes purulent discharge. The filaments are branched and divided much the same as those of the previous forms, and are found in the lesions in the epidermis. In the pustular lesions they are rarely demonstrable.

Epidermophyton inguinale is closely related to the trychophyton fungus and causes eczema marginatum in areas where the skin is approximated and may be macerated by sweat or secretions, e.g., in the popliteal space, axillæ and about mammary glands, anus and genitalia.

Microsporon (**Sporotrichon** of the botanists) **Audouini.** This is found almost exclusively in children and produces localized areas of baldness. An inflammatory reaction of the affected areas is almost always lacking, or, if it occurs, is far milder than that in tinea sycosis. This form shows conidii arranged in a linear mosaic, and small fibers in the roots of the hairs. It is differentiated by cultural methods.

Microsporon (Sporotrichon) **Furfur.** (Fig. 85.) The cause of tinea versicolor, a disease of the skin characterized by brownish-yellow superficial flecks which desquamate. In the scrapings from the epidermis many short fibers and conidii may be demonstrated, very similar to those of Achorion but rather larger and more compact so as to be visible with a lower magnification.

Microsporon minutissimum is a very fine, branching form which may cause erythrasma. It is not certain that it has any ætiological significance.

Sporotrichon Beurmanni produces small intra- and subcutaneous abscesses. May be cultured from the pus.

Aspergillus fumigatus and niger are sometimes found in the sputum of tuberculous or phthisical individuals and may also produce a type of pneumonia: **pneumonomycosis.** It is an unbranched filament with double contour and countless, sometimes brownly pigmented, spores. Aspergillus or Mucor is sometimes found in the external auditory canal, in the nose or nasopharynx.

In order to render these forms visible the preparation (obtained from the tongue, from scraping of the epidermis, or from hair, etc.) is mixed with 10% potassium hydroxide and the mixture is slightly warmed for a few minutes; a drop of distilled water is then added to prevent crystalliza-

Fig. 86.—Oidium albicans.

tion. A cover-glass is pressed down over the mass and the excess fluid sucked off. By this means the tissue elements are swollen to invisibility whereas the more resistant mold filaments come sharply into view. Examination should be carried out with a high dry lens without condenser.

Oidium albicans (Monilia candida) (Fig. 86), represents a transitional form from the molds to the yeasts. It is found in the mouth and more rarely in the œsophagus and stomach in the form of white flecks with a slightly reddened area surrounding them. These prove, upon microscopic examination, to be composed of a snarl of branching filaments divided by septa at their points of division, between which lie glistening round or ovoid conidii. They may be cultivated upon weakly acid media containing sugar.

YEASTS

The yeasts, **blastomycetæ,** are ovoid, glistening cells which multiply by the sprouting of a daughter cell from the mother cell as a knob-like protrusion. Upon alkaline media they sometimes form filaments. They ferment sugar to alcohol and carbonic acid and are sometimes found in fermenting gastric contents. The blastomycetæ may sometimes, though rarely, produce disease forming nodular areas of inflammation upon the skin.

Actinomyces, (Fig. 87), is the principal representative of a group of microörganisms intermediate between the penicilia

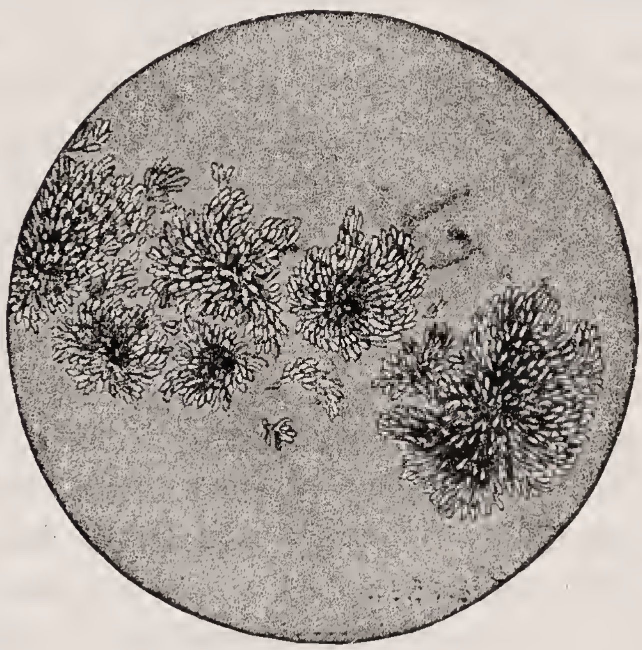


FIG. 87.—Actinomyces

and the streptothrix. It is found in pus in the form of macroscopic yellowish granules the size of a millet seed, which upon microscopic examination show a number of fine radiating fibers with glistening bulbs at their tips. These actinomycotic granules are often calcified and before examination must be decalcified in dilute hydrochloric acid. In some cases no macroscopic granules may be visible. Under these circumstances the suspected pus should be treated as follows: Stain the fixed preparation for 30–40 minutes in warm carbolfuchsin solution, then 10–15 minutes in Lugol's solution, decolorize with alcohol, and wash with water. Branched fibers are characteristic. Artificial cultivation is possible upon appropriate media. Actinomycosis usually arises in the nasopharynx or mouth (carious teeth, or infected tonsils), in the

œsophagus or intestine and may spread from there to involve all other organs; it seems to show a particular preference for the bones. It is characterized by protracted chronic swellings with purulent and destructive lesions.

SCHIZOMYCETÆ

These are the lowest known organisms. They reproduce by simple fission. Most bacteria multiply in a similar fashion, but in certain forms, e.g., anthrax, spore production may take place. Spores represent forms which are more resistant to external influences, e.g., heat, drying, and the action of antiseptic substances, than the growing forms. Dry heat of 150° C. destroys all growth with certainty only after 4 hours; live steam at 100° for 10–15 minutes destroys only the vegetative forms and not the spores. Sterilization may be completed only by prolonged treatment with dilute bichloride solution or 5% carbolic acid. The vegetative forms of most bacteria are destroyed at a temperature of from 52–70° C.

Some microörganisms develop upon dead substrata composed of organic material, e.g., upon animal and vegetable bodies, in the earth and in water. Such are known as **saprophytes** in contrast to the **parasitic organisms** which infest only the living bodies of the higher organisms. Some types, e.g., the anthrax bacillus, may exist as well upon dead substrata as in the animal body: **facultative parasites.** To these parasites belong those bacteria causing most of the infectious diseases, the **pathogenic** microörganisms.

Most microörganisms produce certain chemical changes in their media; thus the putrefaction of protein and the fermentation of alcohol and sugars are due to bacterial action. Certain types liquefy gelatine and other media in that they break these down to peptones; certain bacteria produce gas or pigment, e.g., staphylococcus aureus produces a golden-yellow, micrococcus prodigiosus a bluish-red, and bacillus pyocyæneus a blue pigment.

In addition certain bacteria, e.g., **putrefactive** organisms, produce basic substances (amines, diamines, and ammonium bases), which are known as **ptomaines,** e.g., cholin, neurin, muscarin, cadaverin (pentamethylendiamin), putrescin (tetramethylendiamin), etc. The toxins of many pathogenic

bacteria are infinitely more poisonous than the ptomaines of the putrefactive group. These **toxins** are in part true secretory products of the bacteria. Of their chemical constitution little is known, but they are elaborated by certain microörganisms in artificial media as well as within the living body. The action of many pathogenic microörganisms is, for the most part, to be explained by the fact that the poison which they produce causes injury and necrosis of the tissue in their neighborhood bringing about inflammation. These poisons may gain access to the circulation and affect the entire organism; they are thus accountable for the most varied manifestations of disease, among others fever. So, for example, diphtheria bacilli, growing in the pharynx, elaborate toxins, which, upon absorption into the body fluids, lead to severe symptoms of disease and even to paralyses. Diphtheria and tetanus bacilli produce a sort of toxin which is demonstrable in the culture medium and is known as **exotoxin.** In the case of other bacteria, e.g., typhosus, cholera vibrio and B. pestis, no toxic material may be demonstrated in culture. It is to be assumed that the specific poisonous material of these organisms is contained within the bacterial cell and is set free only upon the death and autolysis of the bacterium (**endotoxin**). The differentiation between exotoxins and endotoxins is made difficult by the fact that many bacteria undergo autolysis in culture.

Morphologically microörganisms are divided into 3 classes.

Micrococci: round or ovoid; according to whether they exist as individuals or in pairs they are spoken of as **mono-** or **diplococci.** If they are arranged in chains they are known as **streptococci;** if they tend to accumulate in groups they are called **staphylococci.**

Bacilli-rods. Many rod forms have the tendency to grow into long fibers or filaments. **Leptothrix** fibers, for example, are long filamentous rods which are often found at the root of the teeth or in the tonsillar crypts and occasionally in chronic bronchitis; they stain with Lugol's solution a beautiful violet and are not to be classified among the simple yeasts.

Spirilli or coil forms, are short, coiled organisms shaped like a portion of a corkscrew; they are also designated as

vibrio. (These forms are to be distinguished sharply from the genuine corkscrew forms, the spirochætæ.)

Many types of bacteria show active motility apparently dependent upon flagella, the arrangement of which is more or less characteristic for each type. To examine for motility and characteristics in fluid culture one employs the method of the "hanging drop": About the depression in a hollow-ground slide is placed a small amount of vaseline and the preparation, made by placing a small drop of the fluid culture upon the center of a cover-glass with a platinum loop, is pressed down over the concavity. Sometimes it is necessary to mix the culture with a drop of normal salt solution.

EXAMINATION OF SMEARS

For purposes of clinical diagnosis in examining pus, blood or sputum for microörganisms the smear preparation and bacterial cultures are most useful.

Preparation of the Smear

A small drop or particle of the substance to be examined (pus, sputum, etc.) is placed upon a clean slide and spread with a platinum loop. When it is not important to determine the relative position of the bacterial clumps a second slide may be pressed upon the first and then carefully drawn off so that the material is spread in a thin sheet. The preparation is then allowed to dry completely in the air and is then passed two or three times quickly through a Bunsen flame. If desirable the dried preparation may be fixed upon the slide by placing it for three minutes in absolute methyl alcohol or in a mixture of equal parts of alcohol and ether; this is of particular importance in staining malarial plasmodia, spirochæta pallida or intracellular bacteria.

Staining the Dry Preparation

According to Ehrlich, stains are divided into 2 classes:

Acid dyes, the staining principle of which is an organic acid, e.g. phthalic acid. Among these the most common are: eosin, picric acid and acid fuchsin. They are used particularly in staining red blood corpuscles.

Basic dyes, in which the staining principle is an organic base, e.g. anilin. Of these the most commonly employed are: fuchsin (rose anilin hydrochloride), methylene blue, methyl violet, gentian violet, Bismarck brown, and malachite green. The basic dyes stain the cell nucleus deeply and stain most microörganisms as well. These stains should be kept in the form of a concentrated alcoholic solution prepared by mixing an excess of dry dye with alcohol in a small flask, thoroughly shaking and, after several days, filtering. Bismarck brown is better prepared as a supersaturated solution in aqueous glycerine.

Before using, stock solution is diluted to one fifth with water. This solution is fairly stable. In staining the preparation is fully covered with the liquid and gently warmed over a flame. Staining is complete in one minute at most. Methylene blue has the advantage that it does not overstain and produces no precipitate; it is, therefore, particularly valuable in staining albuminous preparations. When the preparation is sufficiently stained it is washed until the water removes no more dye and is then dried between layers of filter paper.

For the microscopic examination of such a stained preparation the condenser diaphragm on the microscope is opened wide; by this means the contours of the preparation itself are somewhat blurred and in contrast the stained portions, e.g. bacteria, stand out more distinctly. With unstained preparations, on the other hand, in which it is necessary to distinguish sharply the structural contours, the condenser diaphragm should be partially closed. In searching for bacteria it is necessary to use the highest power, preferably the oil immersion.

The following additional staining methods may be mentioned:

Lœffler's methylene blue. The cover glass preparation is stained for 5 minutes in the following solution: 30 c.c. of a concentrated alcoholic solution of methylene blue, 1 c.c. of a 0.01% potassium hydroxide solution. The preparation is then washed with water, or if necessary, decolorized with alcohol to which a drop of dilute acetic acid has been added.

Anilin-gentian violet or **Fuchsin solution:** 4 c.c. of anilin are mixed with 100 c.c. of water, shaken and filtered. To

10 c.c. of this filtrate are added 20 drops of a concentrated alcoholic solution of gentian-violet or fuchsin.

Ziehl's solution: 100 c.c. 5% carbolic acid solution, 10 c.c. alcohol, 1 gm. fuchsin. This solution is very stable and particularly useful for differential staining in a dilution of 1 : 4 or 1 : 10.

Of particular importance for diagnostic purposes in the presence of a variety of bacteria is the **Gram stain.** A small quantity of anilin oil is shaken thoroughly with 20 c.c. of distilled water and filtered, and a small quantity of gentian violet is added, (or 16 c.c. saturated gentian violet plus 84 c.c. of 5% anilin water. Ed.) After thorough shaking the solution is ready for use; it reaches its maximum staining capacity after about 24 hours and, if kept in a closed vessel, retains it from 2–4 weeks. Much more stable is a solution of phenol and gentian violet (concentrated alcoholic gentian violet solution 10 parts, 2.5% phenol solution 90 parts).

With this solution the preparation is stained for 1–2 minutes, washed, and treated with Lugol's solution (iodine 1.0, potassium iodide 2.0, distilled water 300). This mixture is poured off and the preparation is rinsed with 96% alcohol until the blue color disappears. It is then counter-stained with aqueous fuchsin solution (or saffranin), rinsed and dried. The so-called **gram-positive** bacteria are thereby colored a deep blue while the others (**gram-negative**) are stained red. Staphylococci, streptococci, pneumococci, anthrax bacilli, and diphtheria bacilli are gram-positive. Gram-negative organisms are gonococci, meningococci, all bacilli of the typhoid group, Friedlander bacilli, influenza and cholera bacilli.

For staining bacteria in pus or in exudates the **method of Jenner-May** is useful, as described for staining dried blood preparations (page 163). With this method the bacteria and cell nuclei are stained blue, the red blood corpuscles and the granules of the leucocytes red. Preparations which are to be so stained should not be fixed with heat. The method of Giemsa as described on page 163 is also useful for staining many microörganisms.

In the **rapid method of Giemsa** very thin smears are laid in a Petri dish with 10 to 15 drops each of concentrated Giemsa's solution and pure methyl alcohol. After 30 seconds

distilled water is added to cover the slides, the solution is thoroughly mixed and allowed to stand for 3 minutes. The smears are then washed and dried.

Staining of Tubercle Bacilli (Ehrlich's method)

The sputum to be examined is spread against a dark background and small purulent clumps are picked out. These clumps of pus are placed between 2 slides which are pressed together and then drawn out to make a thin smear. The smears are allowed to dry thoroughly in the air and then passed rapidly through a flame. The preparation is next placed in a glass with Ziehl's solution (instead of the Ziehl's solution one may employ an anilin water-fuchsin solution). The vessel is warmed over a flame to steaming; it is sometimes better to heat the Ziehl's solution in a test-tube beforehand. Under these conditions the preparation is usually sufficiently stained in 5 minutes. It is decolorized for several seconds with acid alcohol (100 c.c. of 70% alcohol plus 1 c.c. of concentrated sulphuric acid) and a half minute in pure alcohol and rinsed with water. If the smear still shows a distinct reddish color this procedure must be repeated until it is only faintly red. By this means, through the action of the acid all bacteria are decolorized except the tubercle bacilli, smegma and lepra bacilli. The smear is then counter-stained with methylene blue or malachite green, washed thoroughly with water, dried slowly over a flame and mounted in cedar oil or Canada balsam. Decolorization and counter-staining may be accomplished in a single procedure by placing the preparation for 3–5 minutes in Frænkel-Gabett's solution: 100 parts of 25% sulphuric acid, 1–2 parts of methylene blue. It is generally more advisable first to decolorize and then to counter-stain.

By this method the tubercle bacilli, smegma or lepra bacilli, alone are stained red and all other organisms green or blue; the tubercle bacilli sometimes show clear spaces in them or appear as a row of fine granules. They may be recognized at a magnification of 350 diameters but the oil immersion is really necessary for an accurate diagnosis. Lately the recognition of the tubercle bacilli has been considerably facilitated by the dark field method.

In the event that bacilli be present in too small numbers

to be demonstrated by the methods outlined above the procedure of Uhlenhuth is often of value. A portion of the sputum is mixed with 2 parts of **anti-formin** (a mixture of sodium hypochlorite and caustic soda), well shaken and allowed to stand for 20 minutes. The homogeneous mixture is mixed with an equal volume of alcohol and centrifuged. The sediment is fixed upon a slide, and stained. The tubercle bacilli are to be found in the sediment; the other bacteria are killed and dissolved. In examining urinary sediment for tubercle bacilli it is often difficult to make the preparation stick to the slide; this may be accomplished by adding a little egg albumin.

If tubercle bacilli cannot be demonstrated by staining, a specimen of the suspected material may be injected under the skin of a guinea-pig; if tubercle bacilli are present the animal dies within 4-6 weeks and the regional lymph glands are swollen and caseous.

METHODS OF BLOOD CULTURE

In many infectious diseases, and particularly in sepsis, typhoid and pneumonia, the demonstration of the causative agent in the blood is of great clinical significance. After thorough cleansing of the skin 15–20 c.c. of blood are withdrawn by vena-puncture from the cubital vein into 4 c.c. sterile 2.5% citrate solution. Two c.c. of blood are added to each of four test-tubes of pH 7.4 agar (one of glucose agar) which has been previously melted and cooled to 42–45° C. After mixing plates are poured in sterile Petri dishes. The remainder is planted in dextrose broth. The cultures are then incubated from 24–48 hours but should never be discarded earlier than the 8th day; in cases in which streptococcus infection is suspected they should be kept for 3 weeks.

Protection Against Infection

It appears that to certain infecting agents all human beings are equally susceptible: e.g., those of gonorrhœa and syphilis, cholera, plague, whooping cough, mumps and influenza. Thus, if one of these diseases appear in a household all the individual members thereof may contract the disease if they are exposed. To certain other infectious diseases only a

portion of exposed individuals are susceptible. This is true above all of tuberculosis, diphtheria and scarlet fever. By means of the **Schick test** it is apparently possible to predict, during a diphtheria epidemic, which individuals are susceptible to the disease and which are not. A small amount (1/50 minimum lethal dose as determined for a 250 gm. guinea pig) of dilute diphtheria toxin* is injected into the skin. If a localized area of inflammation appear about the site of injection after 24 hours the individual is considered to be susceptible. This susceptibility may be overcome by the injection of a combination of diphtheria "toxoid."†

During epidemics of meningitis cerebrospinalis epidemica, or of poliomyelitis, transmission of the disease from person to person is rarely demonstrable. It is to be assumed that the transmission of these infectious agents may be accomplished through a series of intermediate hosts the individual members of which may not themselves present manifest symptoms of disease. The resistance of any individual to an infection may undergo transient or protracted diminution by a variety of intercurrent factors, e.g., malnutrition, chilling or trauma.

Against the action of infecting bacteria and their poisons is arrayed a variety of mechanisms on the part of the organism. In the first place the infecting agent may be ingested by certain cells and thus be rendered innocuous (phagocytosis).

In this relation the polymorphonuclear leucocytes of the blood and pus are most important (**microphages**), but the large mononuclear derivatives of the endothelium may also function in this manner (**macrophages**). The leucocytes ingest many types of bacteria, particularly cocci, e.g., gonococci, meningococci, and staphylococci; the macrophages enclose tubercle bacilli and various foreign cells. In the blood serum of healthy or diseased individuals there are certain substances which so influence the infectious agent as to facilitate its phagocytosis. These are known as **opsonins.**

Secondly, in the blood serum of human beings and of

*Material for performing Schick test is usually available at the office of the local Board of Health.

†Also available at Board of Health.

animals there exist certain substances which are capable of killing certain bacteria or at least of inhibiting their multiplication. These substances are not specific, i.e., they may act against various types of bacteria. They are, in addition, thermolabile, i.e., destroyed by heating the serum above 60° C. Buchner has called these substances **alexins.** If bacteria penetrate into the blood from an infected focus, e.g., during typhoid fever, pneumonia or tonsillitis, they tend to disappear rapidly from the blood stream; presumably they are quickly destroyed under the influence of the alexins or are removed by the endothelium of the blood vessels. In severe cases of infection this protective mechanism may be overwhelmed by the large numbers of bacteria which gain access to the blood stream.

In contrast to these non-specific protective substances are to be distinguished those reactions which develop specifically in the body following the introduction of microörganisms or their toxins, and which afford protection only against the particular infecting agent concerned. Among these substances two groups are distinguished: **antitoxins** which neutralize the bacterial toxin, and **bacteriolysins** which destroy or dissolve the bacterial cells. Such specific protective substances may be developed not only against bacteria or their poisons but also against foreign cells or even foreign proteins. All substances which call forth, upon their introduction into the organism, the production of protective substances, i.e., the elaboration of antibodies, are grouped under the term **antigens.**

Antitoxins. When the toxins of certain bacteria, e.g. diphtheria or tetanus, are absorbed from a focus of infection and gain access to and injure the tissues of the body, there are formed in the tissues certain antibodies, **antitoxins,** which tend to neutralize the bacterial poison. Toxins and antitoxins combine in certain definite proportions to form an innocuous mixture. Antitoxins are highly specific, i.e. they are opposed only to such toxins as may cause their formation in the organism. They may be called forth not only by infection with living bacteria but by **artificial** intoxications, produced by the injection of toxic materials obtained from the bacterial culture. A patient who has recovered from an infection with

diphtheria, or an animal, into which has been injected a certain amount of diphtheria toxin, shows in the blood serum, for a number of weeks thereafter, antitoxins which render them immune to the poison of the diphtheria bacillus, i.e. diphtheria bacilli are no longer poisonous for them, cannot produce the disease in these individuals nor injure their tissues. Inasmuch as the antitoxin is opposed to the poison of the diphtheria bacillus but cannot kill these organisms it is possible for a patient, although he is himself immune to diphtheria, to carry large numbers of diphtheria bacilli in his pharynx and to transmit the disease to other patients ("carrier").

Antitoxins are carried in the blood serum and may be transferred with it to other patients or to animals. Prophylactic immunization is thereby effected against the infecting agent in question, or the disease may be cured or aborted. This transfer of immunity by the injection of serum from an animal treated with toxin (antidiphtheria serum) to man or to another animal, is known as **passive immunization.** By **active immunization** one understands that form which is the result of the production of immune substances within the body itself. Active immunization is far more effective and lasting.

Precipitins. If foreign proteins are injected into the blood stream and are thus transferred to the tissues, they act like poisons and under their influence antibodies are produced. When mixed in a test tube with the protein in question these substances produce a precipitate. If, for example, egg albumin be injected into a rabbit the blood serum of this animal will precipitate egg albumin for some time thereafter. This observation makes possible the identification of foreign proteins: If for example human blood serum be repeatedly injected into a rabbit, after several weeks its serum will produce a precipitate immediately upon mixing with human blood serum. If the blood serum of another animal be added in its place no precipitate is formed; these **precipitins** are specific, i.e., they produce a precipitate only with the blood serum or tissue fluid of the animal under whose influence they have originally been produced.

The following protective mechanisms are directed against the **bacterial cells.**

Agglutinins. Under the influence of an infection with certain types of bacteria, e.g., typhus, paratyphus, dysentery and cholera, there are formed in the infected organisms substances which produce clumping and immobilization of these bacteria in broth culture. Agglutinins are also found in the blood serum; thus, for example, the blood serum of a patient who has or has had typhoid fever, or of an animal into which a culture of B. typhosus has been injected, produces, upon addition to a fresh broth culture of B. typhosus, a flocculent precipitate and agglutination even in considerable dilution, i.e., clumping and sedimentation of the previously actively motile typhoid bacilli. Since this reaction is specific it may also be used for purposes of diagnosis. If, for example, the blood serum of a patient be mixed with a culture of typhoid bacilli, the presence or absence of agglutination serves to determine whether or not this patient suffers from typhoid fever. Such agglutination also occurs with the serum of a healthy individual who has undergone "typhoid inoculation," i.e., into whom killed typhoid bacilli have been injected for purposes of immunization. Or the agglutination reaction may be utilized to identify an unknown bacterial culture. For this purpose blood serum is obtained from an individual who undoubtedly suffers from typhoid fever, or from an animal prepared by the injection of typhoid bacilli. To this serum is added a broth culture of the bacteria in question; if agglutination takes place the culture contains typhoid bacilli, if it fails to appear one is dealing with some other bacterium. In a similar fashion the organisms of paratyphoid, dysentery and cholera may be identified.

Blood serum which specifically agglutinates typhoid bacilli tends to produce a certain amount of agglutination with paratyphoid, B. coli, and related bacteria. The serum of a patient with typhus fever agglutinates certain strains of B. proteus (X 19) which almost certainly have nothing to do with the causation of the disease (para-agglutination) (page 370).

Bacteriolysins are formed in the tissues under the influence of infecting microörganisms and condition **acquired, active immunity.** They are able to counteract and to autolyse only the bacteria under whose influence they have

been brought into existence. If, for example, a guinea-pig be injected with cholera bacilli this animal may become immune against this organism. If, now, after the interval required for the development of immunity (2–4 weeks) the animal receives a dose of virulent cholera bacilli in the peritoneal cavity, the microörganisms are dissolved and disappear within a short time (Pfeiffer's phenomenon). **Fresh** blood serum from such an immune animal mixed in a test-tube with a culture of cholera bacilli brings about the death of these organisms. If, on the other hand, the blood serum be allowed to stand for some time or be heated for a half hour at 56° it becomes inactive. Its bacteriolytic power returns immediately, however, if there be added several drops of fresh serum from any other (not necessarily immune) animal. This bactericidal, and particularly bacteriolytic, action is apparently, therefore, due to two components: The first, which is thermostabile and contains the specific antibody, and the second instabile, thermolabile substance which **is nonspecific** and which acts not only to kill various types of bacteria but to destroy red blood corpuscles in a similar fashion. This second substance is widely prevalent in the fresh blood serum of all the higher animals; since it is indispensable to the activity of the specific immune bodies it was called by Ehrlich **complement.** Since the specific body enters into combination with both the complement and the bacterial cell it was termed by Ehrlich **amboceptor.**

An analogous phenomenon is observed when any foreign cells, in particular red blood cells, are introduced into the animal body (**cytolysins, hæmolysins**). For example, if the red cells of a goat be injected into a rabbit and blood serum be withdrawn from the rabbit after several weeks and mixed in a test-tube with a suspension of goat corpuscles, the latter are broken up, the hæmoglobin is freed and colors the serum. If, however, the rabbit serum be inactivated by heating to 56° C. i.e., robbed of its complement, the dissolution of the goat corpuscles fails to occur, these sink to the bottom and the supernatant serum remains colorless. If, now, a drop of fresh blood serum from another animal, e.g., guinea-pig, be added to the mixture, the goat corpuscles are dissolved as the specific hæmolytic amboceptor combines with the com-

plement which has been added, and is thereby activated. This reaction may be applied for diagnostic purposes, i.e. typhoid fever: A small amount of blood is withdrawn from the patient and the serum obtained by allowing it to stand. If the patient suffer from typhoid this serum should contain specific anti-bodies against typhoid bacilli. The serum is heated to 56° C. to destroy the complement. To this serum, which still contains the specific amboceptor, is added a culture or an extract of typhoid bacilli, i.e. antigen. If, now, to this mixture of amboceptor and antigen be added several drops of fresh guinea-pig serum, containing complement, the complement will be fixed if the blood serum contains typhoid antibodies. However, in case the patient does not have typhoid, but some other disease, his blood serum will not contain the specific typhoid amboceptor, no combination between the antigen (typhoid bacilli) and the amboceptor will take place and the complement remains free. In order to determine this, the phenomenon of hæmolysis, as described above, is employed: To the mixture is added the inactivated serum of a rabbit which has been injected with sheep serum, and a small number of goat corpuscles. If the complement is not fixed but free, there occurs a combination of the complement with the sheep corpuscles and the hæmolytic amboceptor of the previously treated rabbit; the sheep corpuscles are dissolved and the mixture discolored by hæmolysis. If, on the other hand, the patient is in reality suffering from typhoid fever the complement will already have been utilized in binding the typhoid amboceptor and the typhoid bacilli, and there is, therefore, no free complement to bring about the hæmolysis of the sheep corpuscles. In this positive result hæmolysis fails to occur, the blood corpuscles sink to the bottom and the supernatant fluid remains colorless. (See outline, p. 329.)

This principle, discovered by Bordet, led to the development of the **Wassermann reaction** for syphilis. In this reaction an extract of the liver of a case of congenital syphilis is used as antigen. To it is added patient's serum (inactivated by warming to 56° C.) and a small quantity of fresh guinea-pig serum (complement). In the presence of syphilis the complement is bound by the antigen of the serum; if, on the

Hæmolysis absent

If serum come from patient with typhoid, i.e. contains typhoid-antibodies: complement fixed to typhoid antibodies plus typhoid bacilli.

1. Serum (Amboceptor)
2. B. typhosus (Antigen)
3. Fresh guinea-pig serum (Complement)
4. Sheep corpuscles (Antigen)
5. Serum of rabbit previously treated with sheep's blood (Amboceptor)

Hæmolysis present

If serum contain no typhoid antibodies: complement remains free to combine with sheep corpuscles and immune rabbit serum.

other hand, the patient is not syphilitic, i.e. the blood serum contains no specific amboceptor, the complement remains unfixed. The mixture is allowed to stand for a short time in the water bath so that the fixation may occur and there is then added the inactivated serum of a rabbit immunized to sheep's blood and a suspension of sheep corpuscles. If syphilis is present, i.e. if the serum under examination contains the syphilitic amboceptor, the complement is fixed to this and no hæmolysis of the sheep corpuscles occurs; the supernatant fluid remains colorless. If, on the other hand, the patient is not syphilitic the solution becomes reddened with hæmoglobin, since the complement is free to bind the hæmolytic system.

The Wassermann reaction has proven extremely valuable in the diagnosis of syphilis although the principle is not infallible. On the one hand, an alcoholic extract of a normal, nonsyphilitic organ may bring about complement fixation with the blood serum of syphilitic patients, and on the other, the reaction is sometimes positive in certain diseases other than syphilis, i.e. malaria, leprosy, sarcoma, trypanosomiasis, scarlet fever (and Weil's disease). A negative Wassermann reaction is, therefore, not indisputable evidence of the absence of syphilis. The Wassermann reaction involves considerable technical difficulty and requires careful control. It is accurate only in the hands of experienced individuals.

In addition to the Wassermann reaction in many laboratories the precipitation reaction of Sachs-Georgi is utilized; this agrees very closely with the Wassermann reaction and is far more simple. An alcoholic extract of the beef heart is mixed with the serum under examination and incubated. After 2 hours there occurs a fine, flocculent precipitate, visible with a hand lens in the syphilitic serum, which fails to appear in the non-syphilitic. The reaction is slightly less characteristic for syphilis than the Wassermann and its principle, though not yet entirely clear, may prove to be related to that reaction.

In any infectious disease there may develop an active acquired immunity which may endure for months, years, or even for the lifetime of the individual. So, for instance, an attack of variola protects a patient for life; scarlatina, whooping cough, varicella and pappataci fever produce an immunity practically as effective. In the case of typhoid and measles protection is not so perfect while in cholera, relapsing fever, typhus, plague and diphtheria immunity lasts only for a few years. In certain other diseases, e.g., pneumonia, influenza, articular rheumatism and various types of streptococcus infection no such protection can be demonstrated. In the first class of diseases immunity is produced even by a very mild attack. It is this principle which makes possible effective protection against small-pox by vaccination with cow-pox.

On the other hand, the development of an infection in certain cases produces an alteration in the reaction of the organism to the disease agent involved (**allergy** of von Pirquet). Thus with the first inoculation with cow-pox serum the inflammatory reaction reaches its maximum in from 9–11 days, upon repeated inoculation this occurs on the 4th or 6th day. About the first vaccination there develops a circumscribed necrosis of the skin which leads to scar formation, whereas with the second inoculation this is absent. Of particular importance is the fact that recovery from an infection or intoxication may leave the individual in a condition of **hypersensitivity** (**anaphylaxis**). Thus an animal which has been inoculated with diphtheria bacilli may become so extremely sensitive that the second injection of a

very small quantity of diphtheria toxin may prove fatal. This hypersensitivity is of particular significance in tuberculosis. While it is possible for a patient or an animal to survive the injection of relatively large quantities of tuberculin without injury, an individual already infected with the disease develops a local inflammatory reaction about an old tuberculous focus as well as about the point of injection, and a generalized febrile reaction even upon the injection of a fraction of a milligram of this substance. It is upon such hypersensitivity that the diagnostic tuberculin test depends. This condition is also important in the case of injection of heterologous serum since the patient, while he may suffer no ill effect from the injection of horse serum containing diphtheria antitoxin, may, upon a second injection of horse serum containing, perhaps, some other antitoxin, suffer from alarming constitutional symptoms, urticaria, œdema, pain and swelling in the joints, fever or subnormal temperature and collapse (**serum disease**).

While the first injection into an animal of a foreign protein, e.g., an heterologous serum, may be unattended by reaction of any sort a second subcutaneous injection two weeks later may bring about violent inflammation or necrosis at the site of injection (Arthus' Phenomenon).

Allergy is apparently of fundamental importance in the development of certain forms of disease, e.g., bronchial asthma and hay fever, which develop following the inhalation of certain pollens.

Summary of the Most Important Microörganisms and Infectious Diseases

Staphylococcus pyogenes aureus (Fig. 88). A round coccus which tends to clump. Grows upon gelatine, which it liquefies at room temperature, and upon many other media; its colonies are distinguished by a round colorless cap upon each, by their luxuriant growth, and by their golden-yellow color. Staphylococci stain with all the anilin dyes, and are gram-positive. They are widely distributed in our environment, appear almost universally upon the human skin, and are, therefore, commonly found in cutaneous pustules. Staphylococcus is the most common pyogenic organism and is

found in abscesses, phlegmons, purulent arthritis and, more rarely, with inflammation of the serous surfaces. In pyemia it is widely distributed in the body and may be demonstrable in the blood; it is occasionally met with in the valvular lesion of endocarditis and with great regularity in acute osteomyelitis. In otitis media, in acute or chronic bronchitis, and in pyelitis it is often found in the secretions. Finally, it not uncommonly appears as a secondary invader in other infectious diseases, e.g., in the contents of variola pustules.

In addition to aureus another staphylococcus is sometimes found in pus, **staphylococcus pyogenes albus,** which is distinguished from aureus by the absence of yellow pigment

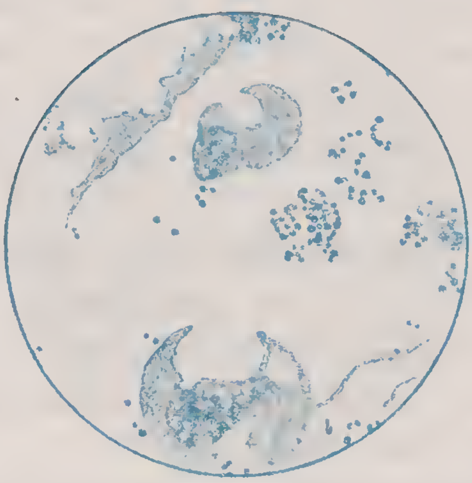


Fig. 88.—Staphylococcus pyogenes aureus in pus.

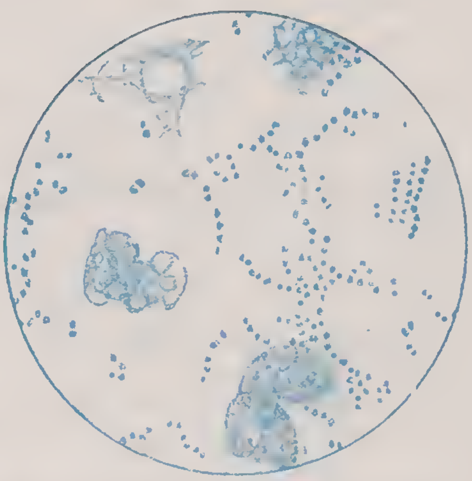


Fig. 89.—Streptococcus pyogenes. (Pus from abscess.)

in its colonies. A third type, S. pyogenes citreus does not liquefy gelatin. The pathogenic staphylococci are distinguished from the numerous non-pathogenic forms by the fact that, in culture, they produce hæmolysis, i.e., form an hæmolysin.

Streptococci. Streptococcus pyogenes (Fig. 89), round cocci arranged in chains. In pus, in the blood in sepsis, in and about the tonsils in angina, and in many pathological fluids they form either diplococci or very short chains; in broth culture they grow in long chains. Streptococci grow at room temperature on all media and upon gelatine, which is not liquefied, in the form of small transparent colonies. Cultures lose their virulence rapidly. Easily stained with all basic anilin dyes; gram-positive.

The streptococcus pyogenes is found in many purulent

processes, in tonsillitis or pharyngitis, endocarditis, puerperal sepsis, and in pleurisy, particularly with empyema. It may also appear as a secondary invader, e.g., in grippe, in many cases of diphtheria in association with the diphtheria bacillus, and in practically all inflammatory and purulent complications of scarlatina. Streptococcus infections are often very severe and malignant. Finally, it is regularly encountered in erysipelas in the portions of the skin most recently involved, and in the purulent processes which follow erysipelas; on the other hand, it is rarely found in the vesicles of erysipelas.

In addition to the pathogenic virulent forms of streptococci non-virulent forms are widely distributed in our environment and are found as harmless inhabitants of the pharynx, upon the tonsils, in the vagina and upon other mucous membranes of healthy individuals. These non-pathogenic forms may sometimes be differentiated from the pathogenic types only with difficulty. Differentiation by means of mouse inoculation is often useful but not necessarily certain since many forms which are pathogenic for man produce no disease in animals and vice versa.

Saprophytic streptococci grow luxuriantly and cause no change in the blood plate.

Streptococcus pyogenes commonly found in pus in the other diseases mentioned above, forms upon a blood plate a clear colorless halo about its colony; i.e., is hæmolytic (streptococcus hæmolyticus).

A less common form, **streptococcus mitior or viridans,** occurring usually with chronically progressing disease and particularly with endocarditis lenta, forms no halo of hæmolysis but colors the media in its neighborhood a dark green. It is only moderately pathogenic for animals. It is frequently encountered in cultures from the mouth or pharynx and is here of no serious significance. These streptococci sometimes invade the blood stream particularly in cases of chronic endocarditis. Such viridans septicæmia commonly leads to death with irregular fever, endocarditis, arthritis and sometimes focal nephritis.

Streptococcus putridus is strictly anærobic, non-hæmolytic and produces gas (H_2S). It is found in cases of abortion

with sepsis and in alveolar abscesses. It is characterized by the production of a foul odor in pus and in culture. The more virulent the streptococci the less are they taken up by the normal human leucocytes. Burger has suggested a method for determining the virulence of streptococcus strains by the degree to which they undergo phagocytosis.

Erysipelas has an incubation period of 1–3 days. Onset usually with chill and high fever. On the first or second day inflammation of the skin appears. The temperature remains high as long as the inflammatory process spreads and falls rapidly as it subsides. In some cases the skin lesion spreads, step by step, and is accompanied by an irregularly remittent or intermittent fever. Erysipelas of the face usually starts from the nose. Nephritis is sometimes a sequel.

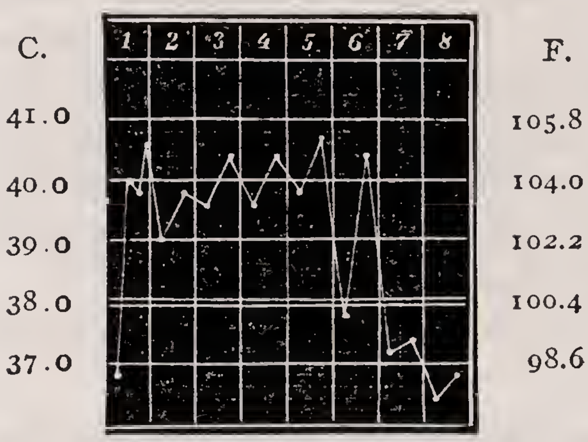


Fig. 90.—Temperature chart in erysipelas.

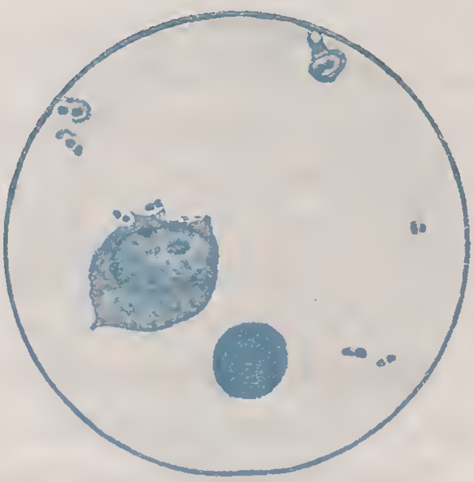
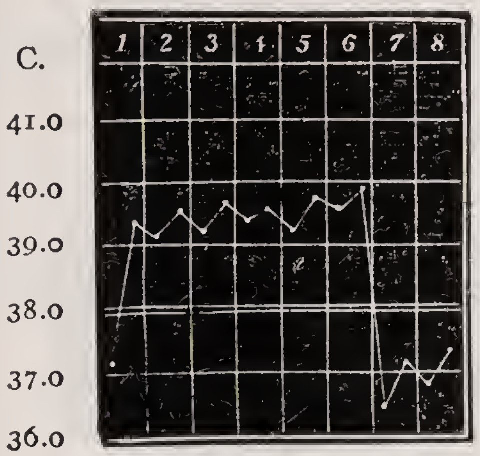


Fig. 91.—Pneumococcus (A. Fraenkel). Pneumonic sputum.

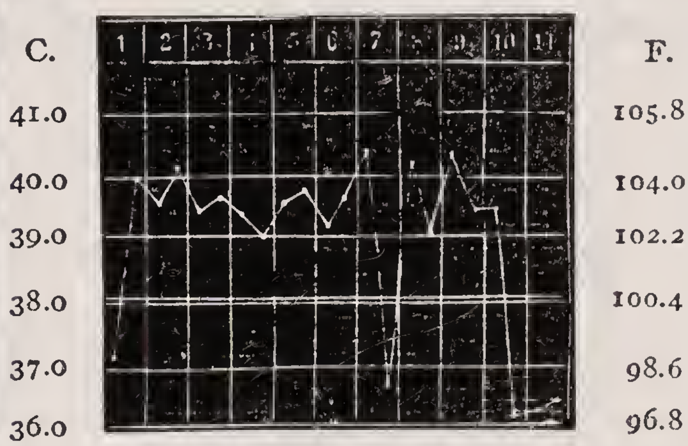
Pneumococcus (A. Frænkel) (Fig. 91). In lobar pneumonia are found, in the consolidated portions of the lung, and in the sputum, large numbers of cocci, usually in the form of diplococci which are often ovoid or lancet-shaped. In the sputum and in the lung this organism is surrounded by a capsule but this is not seen usually in culture. The pneumococcus is frequently to be identified by the characteristic shape. It grows only at 37° upon blood-agar, blood serum or bouillon; the cultures quickly lose their virulence. It is very virulent for rabbits and mice, less so for guinea-pigs. It stains with all anilin dyes and is gram-positive. It may be demonstrated by subcutaneous injection into a mouse; the animal usually dies in 24–48 hours and the organism may be demonstrated in its blood. (A perhaps more certain method

is the intraperitoneal inoculation: Wash sputum in sterile saline to remove mucus, grind in sterile mortar and emulsify with sterile saline. Inject 1–2 c.c. of the mixture into peritoneum of a mouse. The animal usually dies in 12–24 hours. Typing may be carried out upon a saline emulsion of the peritoneal exudate, which contains pneumococci in enormous numbers. Ed.) This organism is also found in many normal sputa, in post-pneumonic empyema, in some cases of cerebrospinal meningitis, with endocarditis and otitis media. In severe pneumonia it may sometimes be demonstrated in the blood. It is distinguished from streptococcus viridans by its lancet-shape, capsule-formation, the intensive greenish



Crisis.

FIG. 92.



Pseudocrisis.

FIG. 93.

Temperature charts of lobar pneumonia.

coloration which it produces upon a blood plate, (and its solubility in bile. Ed.)

American authors have recently distinguished 4 types of pneumococci which are separated by their agglutination and precipitation reactions. Anti-sera have been developed against types I and II only.

Friedlander described an encapsulated bacillus in lobar pneumonia which grows upon gelatine, at room temperature, without producing liquefaction, and is pathogenic for rabbits. This organism is found in only a very small percentage of cases of pneumonia. Streptococcus mucosus is also present in some cases of pneumonia.

Lobar pneumonia usually begins with chill and sudden rise in temperature. Soon there develops sharp pain in the side and cough, with a production of rusty sputum. Fever usually

continuous during the early stage of the pneumonic infiltration. On the 7th day or thereabouts, the temperature suddenly falls with a profuse sweat and coincident slowing of the pulse and respiration (**crisis**). Sometimes the crisis is preceded by a day or two by a pseudo-crisis during which the pulse and respiratory rate remain high. When the temperature falls gradually over several days one speaks of defervescence by **lysis.** Sequelæ: Pleurisy with effusion or empyema.

Meningococcus (diplococcus intracellularis meningitidis of Weichselbaum) (Fig. 94), biscuit-shaped diplococci usually contained within leucocytes and microscopically very similar to gonococci. Stain with all anilin dyes and are gram-negative. Grow only at body temperature and best upon media containing human serum, e.g. blood agar and ascitic-fluid agar.

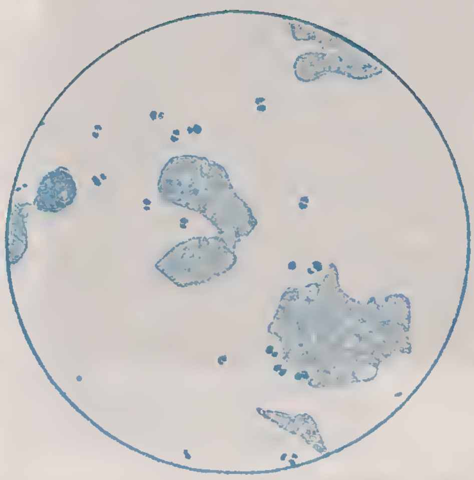


Fig. 94.—Meningococcus intracellularis. Pus from meninges.

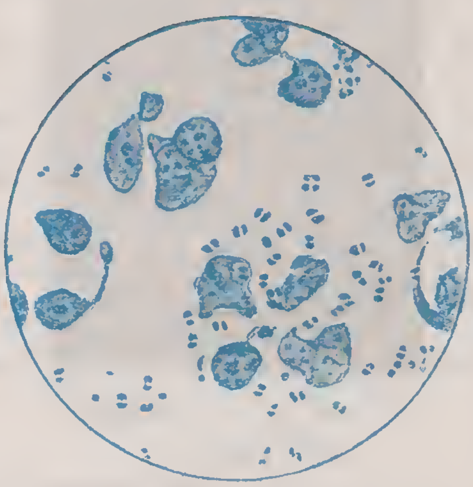


Fig. 95.—Gonococcus (gonorrheal pus).

Cultures die out rapidly. In pure cultures the cocci appear in pairs or in fours. Relatively non-pathogenic for animals. Meningococcus is found with great regularity in the secretion from the nose and naso-pharynx of patients with cerebrospinal meningitis, of which this organism is the cause. The blood serum of a meningitic patient agglutinates the cocci. The recovery of meningococci from the cloudy or purulent spinal fluid obtained by lumbar puncture is of diagnostic significance (see page 240). In the spinal fluid it is sufficient to demonstrate that the cocci are biscuit-shaped and that diplococci and intracellular cocci appear. These organisms are distinguished from pneumococci by the fact that they are gram-negative. Meningitis is spread principally by so-called "meningococcus carriers," i.e., individuals who harbor the

organism in the naso-pharynx although they are themselves healthy or at most afflicted only with a mild coryza. In suspected cases the mere identification of a gram-negative diplococcus in the nasal secretion is not sufficient, since the benign micrococcus catarrhalis is of the same microscopic appearance. The meningococcus must be identified by agglutination and cultural methods. In addition to the epidemic cerebrospinal meningitis caused by the meningococcus, other forms of purulent inflammation of the meninges are caused by pneumococcus or more rarely by other organisms such as B. typhosus.

Epidemic cerebrospinal meningitis begins after an incubation period of 1–4 days. The onset is sudden with rapid rise in temperature, headache, vomiting, stiffness of the neck and spine, Kernig's sign (pain upon straightening the knee with the hip joint flexed), delirium, sometimes diffuse herpes facialis. Abdomen flat or scaphoid. Fever irregular, often lasting several weeks. Serious cases run a rapid course to death within 1–2 days.

Pneumococcus meningitis sometimes accompanies otitis media, sinusitis or pneumonia; the symptoms are the same as in epidemic meningitis. **Tuberculous meningitis** is characterized by an insidious onset and course, by the frequency of pupillary changes, extraocular muscular paralyses, and the presence of tubercles in the retina; lymphocytes and tubercle bacilli are sometimes demonstrable in the spinal fluid.

Gonococcus (Neisser) (Fig. 95), cocci, usually paired, and when so arranged their adjacent surfaces are flattened, producing a biscuit-shape; they often fill the entire cytoplasm of certain leucocytes. Culture is only possible when they are inoculated upon warm media directly following their removal from the urethra; they grow only upon blood serum—or ascitic fluid agar. Gonococci stain in the dry preparation with all anilin dyes, best of all with concentrated aqueous methylene blue. They are constantly found in gonorrheal pus, more rarely in conjunctivitis, endocarditis and arthritis. They are also sometimes isolated from epididymitis, pyosalpynx, etc. Their demonstration is of great diag-

nostic significance. Incubation period of gonorrhœa is 2–3 days.

In staining gonococci a drop of pus is streaked upon a cover-glass or slide, dried over the flame, and stained with concentrated aqueous methylene blue or better according to the method of Jenner-May (see page 163). After about 5 minutes the preparation is washed with water, dried and mounted in Canada balsam. Gonococci are distinguished by their morphology, their tendency to clump and to appear within the leucocytes. In contrast to other cocci which occasionally appear in the urinary tract gonococci are **gram-negative.**

Anthrax bacillus (Fig. 96). Thick, large rods; in the dried preparation the ends of the bacilli appear angular or even concave so that between two members of a chain there sometimes appears an oval, clear space. They are present in tissue extract and the blood in cases of anthrax carbuncle and in the spinal fluid in cases of generalized infection. They grow on gelatine at room temperature and upon most of the ordinary media. They liquefy gelatine and, under certain conditions, although not in the body of the living animal, they produce spores. Anthrax bacillus stains with all the basic anilin dyes and is gram-positive. White mice are very susceptible to anthrax and usually die within 24–36 hours after inoculation; after death large numbers of rods are found in the blood, liver and spleen. Cattle, sheep, swine, rabbits and guinea-pigs are also susceptible to anthrax.

Anthrax is usually transmitted to human beings from animals either by the bites of an insect previously infected from an animal or by contact with the hides or hair of affected beasts, by infected rags, rarely by inhalation of dust containing spores, or by the ingestion of infected meat. Infection of the skin (anthrax carbuncle) produces a dark, bluish-red, indurated swelling and infiltration, sometimes with the formation of vesicles, lymphangitis, fever and striking tendency to relapse.

Typhoid bacillus (Eberth-Gaffky) (Fig. 97), short rod with round ends; length about 1/3 the diameter of red blood corpuscle. These show active motility and are apparently furnished with a number of flagella. They grow at room

temperature upon gelatine, which they do not liquefy, and also upon agar, blood serum bouillon and potato. Typhoid bacilli flourish in milk and may exist for a long time in water. They stain with all the common anilin dyes, with Lœffler's methylene blue and Ziehl's carbol-fuchsin. They are found in the intestine, spleen, bile and in the mouth in all cases of typhoid, in large numbers in the urine and, during the first two weeks of typhoid fever, almost constantly in the blood. The typhoid bacillus may be demonstrated in the blood as follows: One to 2 c.c. of blood drawn from the cubital vein are mixed in a test-tube with bouillon or better with sterile ox bile, since these organisms thrive in bile. After 24 hours

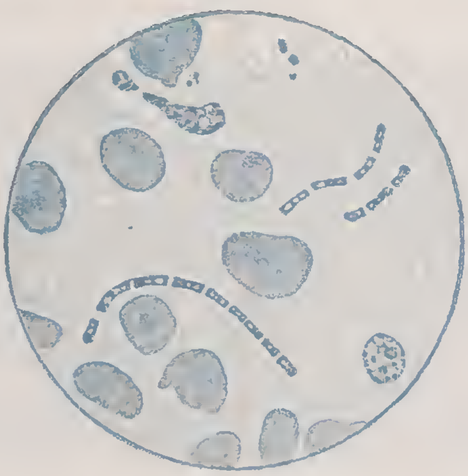


FIG. 96.—Anthrax bacilli. Blood.

FIG. 97.—Typhoid bacilli. Pure culture.

in the incubator the bouillon or bile culture is mixed with agar and plates are poured therefrom. The colonies are then reinoculated into broth, in which, after 12–24 hours the bacilli show active motility. Staining the dry preparation reveals **gram-negative** rods. Or the broth culture may be inoculated upon brom-phenol and substitute agar upon which the typhoid grows blue or upon neutral red-glucose agar: 1000 c.c. water, 10 gm. Liebig's beef extract, 5 gm. of salt, 20 gm. peptone, 5 gm. of agar are heated together for 2 hours, neutralized to litmus, and filtered. Ten c.c. of a concentrated aqueous solution of neutral red and 15 gm. of glucose are then added, the mixture is poured into test-tubes and sterilized. The tubes are inoculated by a deep stab. B. coli colors the agar yellow after 24 hours and, fermenting the glucose, produces bubbles of gas, while typhoid leaves the media unaltered. Final identification is carried out by

agglutination of the broth culture against known typhoid serum.

Typhoid bacilli are usually, but not in every case, demonstrable in the stool; they are sometimes overgrown in the large intestine by other organisms. Since, in the intestinal contents of normal individuals, there appear gram-negative rods which are exceedingly like typhoid bacilli (colon bacilli), the demonstration of typhoid bacilli in the stool demands not only staining and microscopic examination, but also culture upon particular media. For this purpose malachite green agar may be employed, upon which bacteria of the colon group grow less well than the typhoid bacilli, and other organisms grow scarcely at all. Since it has been recently shown that typhoid may be transmitted by carriers, i.e., healthy individuals who harbor typhoid bacilli either in the gall-bladder, intestine, kidney or naso-pharynx, the routine employment of stool culture has assumed greater significance. The typhoid bacilli are distinguished from these of the colon group by the facts that in broth culture they produce no indol, in sugar-containing media form no gas, and in milk cause no fermentation, and further by their blue colonies upon litmus agar in contrast with those of B. coli, which are red.

The more accurate differentiation is the **Gruber-Widal reaction:** This is based upon the fact that the blood or blood serum of patients with typhoid exerts a specific influence upon a pure culture of typhoid bacilli, inhibiting their motility and causing them to group (agglutinate).

The blood serum of a patient is set up in a series of dilutions with physiological saline from 1 : 10 to 1 : 500 and more. From each of these dilutions a drop may be placed upon a cover-glass and mixed with a drop of the broth culture of typhoid bacilli (whereby the serum dilution is doubled). The typhoid cultures should be no older than 14 hours and motile typhoid bacilli should have been demonstrated therein. The cover-glass with this mixture is then placed upon a hollow-ground slide and observed under the high dry lens of the microscope. Agglutination may be observed in the case of a serum from a typhoid patient at once, or after several hours; the typhoid bacilli lose their motility and clump.

The reaction is rarely positive before the 2nd week of the disease but is afterward almost universally so. Particularly significant of typhoid is the fact that a test made early in the disease may be negative or doubtful but becomes strongly positive as the disease progresses. The agglutinating property of the blood serum persists during convalescence and may even last for months or years. This reaction is sometimes of value in locating suspicious carriers in local epidemics.

Practically, agglutination is more easily carried out in small test-tubes containing a series of serum dilutions in saline. To each tube is added a saline suspension of typhoid

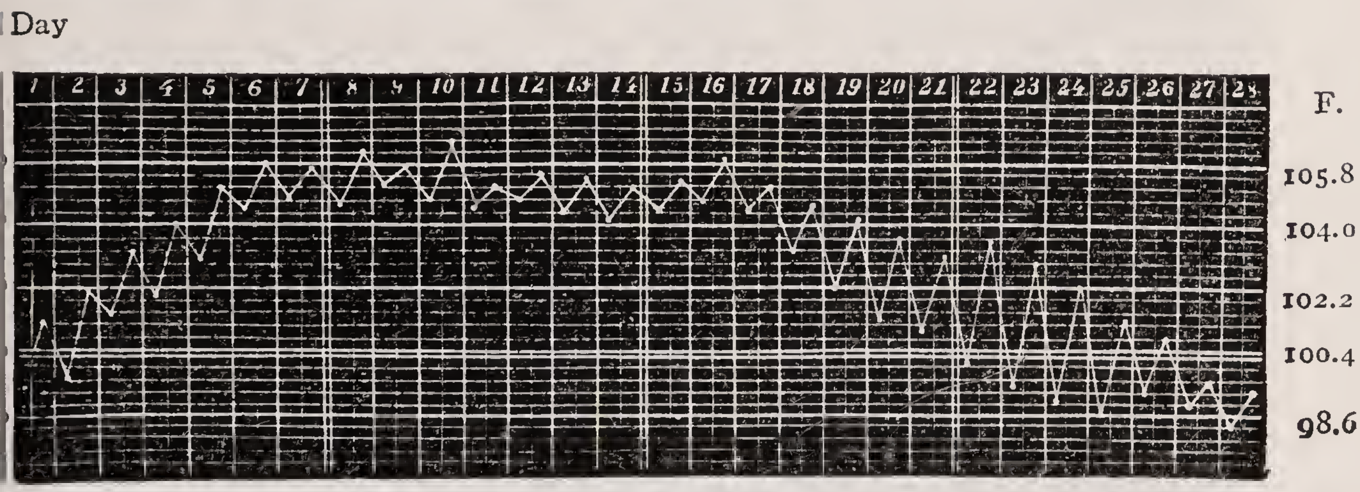


FIG. 98.—Temperature chart in typhoid fever.

bacilli (excepting one tube held as a control). In the usual arrangement the tubes contain serum dilutions 1 : 25 to 1 : 6400. After 2 hours in the incubator agglutination may be recognized macroscopically as a precipitate. It is best to employ a mixture of several strains of B. typhosus. This reaction takes place at room temperature but requires about 24 hours for its completion. The serum for the agglutination test is prepared from blood obtained by vena-puncture from the cubital vein: The blood is allowed to clot and the serum drawn off with a pipette. To this serum is then applied the Gruber-Widal reaction either at the department of health or, if he be so equipped, in the physician's office.

Prophylactic inoculation against typhoid fever is accomplished by 3 injections of at first ½ c.c. and then 1 c.c. of a saline suspension of typhoid bacilli killed by heat at 52°, at intervals of a week to ten days. The injections should be

made subcutaneously and are usually followed by moderate swelling and tenderness at the site of injection, headache and slight rise in temperature. Such prophylactic inoculation vitiates the accuracy of the Widal reaction producing in the individual a high titre of agglutination. It is also a fact that the agglutination titre against B. typhosus sometimes rises during other febrile diseases.

The **incubation period** of **typhoid fever** is from 7–21 days. **Prodromal** symptoms occupy about a week. Onset characterized by headache, general malaise and slowly rising temperature. The temperature reaches the **fastigium** on the 4th to the 7th day and remains continually elevated, in mild cases until the 3rd, and in more severe cases until the 5th week or longer. The morning temperature then tends to be somewhat lower but the evening temperature is quite high; subsequently the temperature falls gradually by **lysis** (defervescence). Bonchitis, sometimes enlargement of the spleen, in the latter half of the first week of the disease; roseola and positive diazo-reaction 6th–9th day of disease. Distended abdomen, sometimes diarrhœa, apathy, delirium, stupor, dry tongue, no herpes, relapses frequent. The blood count shows, from the beginning of the disease, a characteristic reduction in the white blood corpuscles (leucopænia 2000–5000) usually total absence of eosinophilic leucocytes. Complications: Intestinal hæmorrhage, intestinal perforation (accompanied by a sudden leucocytosis), pneumonia, occasionally heart failure.

Paratyphoid bacilli are constantly found in a typhoid-like disease as well as in certain cases of meat and fish poisoning. Paratyphoid fever runs a course similar to, but less severe than, that of typhoid. The symptoms are in general those of typhoid fever but there is often a more pronounced tendency to vomiting and diarrhœa. B. paratyphosus is morphologically and culturally very similar to B. typhosus, is also motile, does not coagulate milk and does not form indol; in contrast with B. typhosus it forms gas in sugar-containing media. It is extremely pathogenic for guinea-pigs and mice. Two types of paratyphoid bacilli are distinguished of which type A is apparently closer to B. typhosus and, like it, grows upon potato medium in the form of a thin veil. Paratyphoid B is less similar to typhoid, and rather more like the colon bacillus, growing upon potato medium as a thick grayish-

brown sheet. Certain cases of severe febrile gastroenteritis with vomiting and diarrhœa, occurring after the ingestion of infected meat, are apparently caused by paratyphoid B.

B. coli commune (Escherich) (Fig. 99): Slim and sometimes slightly bent rods which grow upon gelatine without liquefaction at room temperature and also form a grayish-brown thick sheet upon potato. They produce gas in glucose-containing agar and in media which contain milk sugar (and red color if litmus be present); in addition they produce indol and for this reason emit, in culture, a fæcal odor. They stain with all the anilin dyes, but are gram-negative; are morphologically similar to the typhoid bacilli but are not motile. B. coli are normally present in the large intestine and

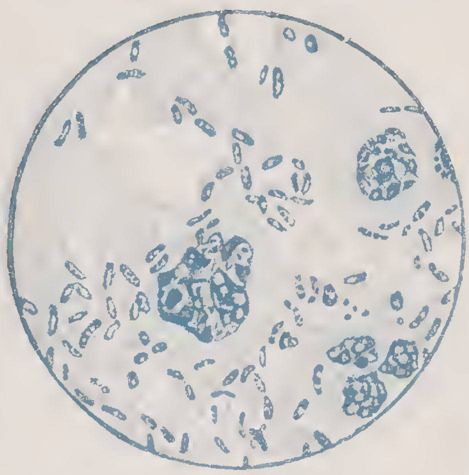


Fig. 99.—B. coli commune.
Pus from peritonitis.

play a part in all inflammatory processes which spread from the bowel e.g., appendicitis and the accompanying peritonitis, as well as inflammation of the gall-bladder and bile passages, liver abscess, and finally cystitis and pyelitis. In the early stages of acute pyelonephritis the urine shows a heavy albumin content, blood and leucocytes, in the later stages the albumin and pus diminish and the red blood corpuscles disappear. Colon bacillus cystitis and pyelitis are characterized by a faintly acid urine; the urine is ammoniacal (and hence alkaline) when the bladder is infected with B. proteus or staphylococci or other bacteria which decompose urea. Bacteriuria (bacilluria) is a condition in which a weakly acid, faintly cloudy urine is voided containing large numbers of colon bacilli; at the same time there is no evidence of

inflammation of the bladder. B. coli are demonstrated bacteriologically by the same methods as B. typhosus.

B. dysenteriæ. In tropical dysentery amœbæ are usually found (page 300) but the local forms of dysentery are to a large extent caused by the bacillus of Shiga and Kruse which are morphologically and culturally closely related to B. typhosus except that they are plumper and non-motile. They are demonstrable in the mucoid, bloody stools of the dysentery patient and may be cultured upon the same media as typhoid bacilli. Since these organisms are easily destroyed cultures are best made by removing mucus with a swab through a proctoscope and planting at once upon blood agar. The bacteria-free filtrate of cultures of this organism contains a toxic substance, which in rabbits and other animals produces paralysis and diarrhœa. Blood serum from dysenteric patients agglutinates this bacillus as does also the serum of animals into which the organism has been injected. In addition to the dysentery bacillus of Shiga and Kruse a second organism has been described by Flexner which produces a somewhat milder form of colitis. This organism produces no soluble toxin and is distinguished from the Shiga-Kruse bacillus by the fact that it grows red upon litmus-maltose agar, whereas the Shiga-Kruse bacillus shows blue colonies; the two organisms are also distinguishable by agglutination. Closely allied to the Flexner bacillus is the bacillus Y which is culturally somewhat different from Flexner's type but indistinguishable by agglutination. Like the Flexner organism it produces no toxin. The cases of dysentery among the German troops in France were in greater part caused by the Y bacillus, whereas the much more severe epidemics in Galicia were due to the Shiga-Kruse organism. Bacillary dysentery is a febrile, infectious disease characterized by violent tenesmus and bloody mucoid stools; tropical dysentery (amœbic) shows rather more the symptoms of a chronic ulcerative colitis.

The **incubation period** of **bacillary dysentery** is from 2–7 days. Sequelæ: Arthritis, more rarely polyneuritis. Amœbic dysentery, **incubation period** 21–24 days. Sequelæ: Gastro-intestinal disturbances, abscesses in the liver, lung or brain which may last for years. In both forms of dysentery, and in

contrast usually to typhoid, the abdomen is tender along the course of the large intestine.

The bacilli of typhoid, paratyphoid and dysentery together with the colon bacillus form a general group and between them there seem to be numerous transition forms. To distinguish the various types, all of which are gram-negative and microscopically and culturally very similar, agglutination methods may be employed, e.g., a culture of gram-negative organisms suspected of containing B. typhosus may be tested against a known typhoid serum. If typhoid bacilli be present they will be agglutinated even in great dilution. It is, however, a fact that the blood serum of an individual who has passed through an infection with one type of these organisms shows a certain amount of agglutinating power against all the other types.

In America **Russel's double-sugar agar** is commonly used for rapid identification of typhoid, paratyphoid and dysentery bacilli. The medium consists of 2–3% meat infusion agar to which have been added 1% of Andrade solution (0.5% aqueous acid fuchsin 100 c.c., normal NaOH 16 c.c.), 1% lactose and 0.1% glucose. Slanted tubes are inoculated both on the surface and by a stab in the depth, and incubated 24 hours. Typhoid, paratyphoid and dysentery produce colorless growth on the surface, but under the conditions of partial anærobiosis at the bottom of the stab, a pink color is produced by the formation of acid. Colon bacillus and paratyphoid form gas in the depths of the tube by fermentation of glucose. The reactions are summarized in the accompanying table:

	Surface	Butt	Gas
B. coli	Pink	Pink	+
B. typhosus	Colorless	Pink	0
B. paratyphosus	Colorless	Pink	+
B. dysenteriæ	Colorless	Pink	0

—Ed.]

Tubercle bacilli (Koch) (Fig. 100), slim rods about 5 μ in length, grow only at body temperature upon blood serum, glycerine agar or broth; they grow very slowly, developing only after several weeks; they are stained by the methods described above (page 321). Wherever tubercle bacilli are

present in the tissues tuberculosis results. The organisms appear in the sputum in pulmonary tuberculosis, in the stool in tuberculosis of the intestine, in the urine in urogenital tuberculosis, in the lumbar spinal fluid in tuberculous meningitis, in the pus of tuberculous disease of the bone or lymph glands, in the blood in disseminated and miliary tuberculosis, and in the skin in lupus and other forms of cutaneous tuberculosis. Guinea-pigs, rabbits, cattle and other animals are very sensitive to the disease. If "tuberculin" (the glycerine-bouillon culture concentrated by evaporation to 1/10 its volume and filtered) be injected into a tuberculous individual there results about any tuberculous focus an inflammatory reaction, and, in addition, fever and other constitutional symptoms. This "reaction" appears in tuberculous human beings following the injection of 0.1 to 1.0 mg. tuberculin while non-tuberculous individuals may withstand much larger quantities and remain symptom-free. As a diagnostic test this reaction may only be utilized in individuals who show a normal body temperature. One half to one mg. of tuberculin (diluted with salt solution) is injected subcutaneously and the body temperature is measured at regular intervals during the succeeding 24–48 hours. If no rise in temperature occurs a second injection of 2 mg. may be given on the succeeding day. If no febrile reaction follows this second injection one may assume that tuberculosis as a disease is not present. If, on the other hand, the patient reacts to the injection of tuberculin by a rise in body temperature it is highly probable that tuberculous disease is present, **or has previously existed.** The cutaneous reaction of Von Pirquet is performed by scratching the skin superficially through a drop of 50% "Old Tuberculin." A positive reaction consists in the formation of an inflammatory papule. The Von Pirquet reaction gives less accurate results in adults.

[**Intracutaneous tuberculin reaction:** After cleansing the skin on the volar surface of the forearm 0.1 c.c. of 1 to 1000 "Old Tuberculin" is injected into the skin by means of a fine hypodermic needle. One tenth c.c. of normal salt solution is injected distal to this point as a control. A positive reaction consists of an area of induration and inflammation over

0.5 cm. in diameter. In any case of suspected tuberculosis it is advisable to test first with still greater dilutions and to proceed, after several days with more concentrated solution of tuberculin.

Strictly speaking a positive tuberculin reaction indicates hypersensitivity to the protein of the tubercle bacillus. This connotes past **infection** with this organism, but not necessarily that the disease is now active.

In certain cases of disseminated (miliary) tuberculosis the tuberculin test may be negative. Ed.]

Cultures of tubercle bacilli obtained from human tuberculosis prove, upon injection into cattle or rabbits, to be avirulent or they produce only a localized reaction or none at all, while strains of the organism from bovine tuberculosis produce in cattle progressive and fatal generalized tuberculosis. Human and bovine tubercle bacilli are, therefore, distinguishable and show also certain characteristic differences in culture. The bovine organism is sometimes encountered but far less frequently in human tuberculosis. A third, still less virulent type, is found in birds, avian tuberculosis. In certain grasses and in impure milk and butter, organisms very similar to tubercle bacilli are sometimes found. The **smegma bacillus** is morphologically very similar to tubercle bacillus and has many of the same staining reactions. Its discovery in the urine may lead to a false diagnosis of urogenital tuberculosis. This may be avoided by examining catheterized specimens. The smegma bacillus is also less acid-fast, i.e., it decolorizes with acid alcohol more easily than does the tubercle bacillus. A distinguishing staining method is that of Pappenheim: Stain with carbolfuchsin as usual. Pour off the excess dye without rinsing and dip several times in the following solution: Saturated alcoholic methylene blue 100, corallin, 1.0, glycerine 20. Rinse with water and dry. Tubercle bacilli appear red, smegma bacilli blue. Konrich recommends decolorizing with a 10%, freshly prepared, solution of sodium sulphide and, after washing, counterstaining with malachite green (50 c.c. of a saturated aqueous solution to 100 c.c. water).

In the sputa of certain patients with tuberculosis and in the exudate from cold abscesses acid-fast rods are sometimes

not found but certain rod forms appear which, as Much has shown, show here and there granules which stain after a prolonged gram staining. Much claims to have succeeded in transforming these granular forms into true acid-fast rods; he maintains that this is another form of the tubercle bacillus. Tubercle bacilli may be more often found in the sputum by using the antiformin method. Two to ten c.c. of sputum are mixed in a test-tube with 2–3 volumes of a 15% antiformin solution, and shaken. The mixture is then boiled and centrifuged. The sediment is removed, mixed with a little albumin, fixed in the flame, and stained.

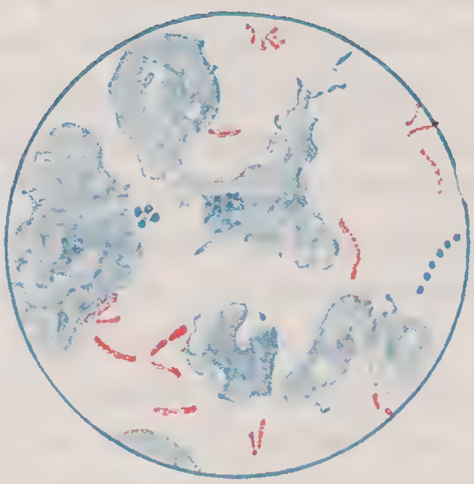


FIG. 100.—Tubercle bacilli. Sputum from pulmonary tuberculosis.

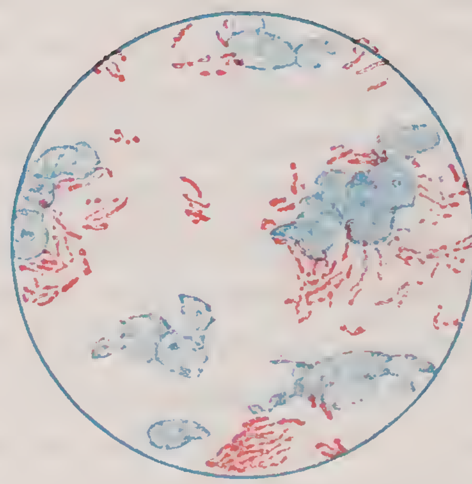


FIG. 101.—Lepra bacilli. Contents of pemphigus vesicle.

Lepra Bacillus (Hansen, Neisser) (Fig. 101), smaller and more delicate than the tubercle bacillus but otherwise very similar. Cannot be cultivated outside the human body; stains by the same method as the tubercle bacillus and, in addition, with the usual anilin dyes; is gram-positive. It is found in all the lesions of leprosy, in the ulcerating skin areas and mucous membranes, in the fæces and tissue fluids in large numbers. The bacilli are usually contained within the so-called lepra cells. These organisms are pathogenic for certain of the lower apes but not for other animals.

Leprosy occurs in two forms: 1. As nodular flecks and nodes upon the skin and mucous membrane, Facies leonina. 2. Similar cases which show also neuralgia and sensory disturbances, particularly in the extremities. Mutilation of the fingers and muscular atrophy similar to that of syringomyelia.

Bacillus of glanders (Lœffler) (Fig. 102), also similar to the tubercle bacillus but somewhat thicker; grows at body temperature upon agar, blood serum, or potato medium; stains with all the anilin dyes, best of all with Lœffler's methylene blue, gram-negative. The organisms are demonstrable only in the blood and in the fresh lesions of glanders, not in the lesions which are ulcerating or breaking down. The microscopic examination of pus or secretions from such lesions is, therefore, of less diagnostic value than animal inoculation (mouse or guinea-pig); the male guinea-pig injected with cultures of this organism develops a swelling of the testis. Of diagnostic significance is the agglutination of the killed organisms by the serum of the patient down to a dilution of at least 1 : 1000.

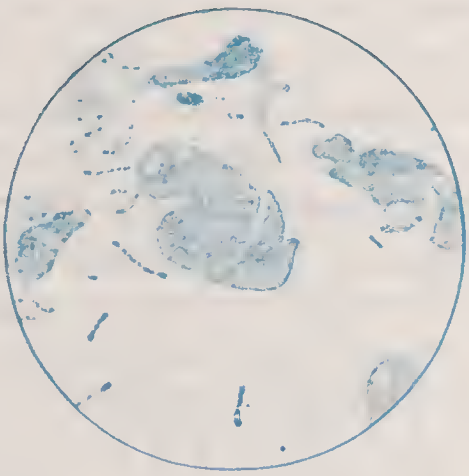


FIG. 102.—Glanders bacilli. Pus from abscess.

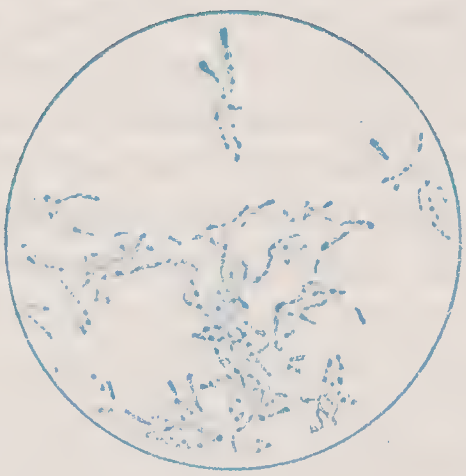


FIG. 103.—Diphtheria bacilli. Pure culture.

Glanders (malleus) is extremely infectious and is transmitted to human beings from diseased horses. After an incubation period of from 3–5 days there appears, in and about the site of infection, redness and swelling which progress to ulceration, lymphangitis and lymphadenitis. Severe constitutional symptoms develop with papular or pustular skin lesions and abscesses in the muscles and viscera. More rare in man is the nasal form characterized by coryza and a thin sanguino-purulent secretion. In such cases the inflammation spreads to the pharynx, larynx and lungs. Glanders is almost always fatal.

Diphtheria bacillus (Lœffler) (Fig. 103). Short, plump, sometimes bent and apparently friable, rods which carry at their ends rounded, deeply staining masses (polar bodies). They are found in groups in the membrane of pharyngeal

diphtheria as well as in the pseudo-membrane of laryngeal and tracheal diphtheria. They do not penetrate the tissues, are very seldom to be found in the blood stream or viscera and then only in small numbers. They grow at body temperature, best of all upon blood serum, and rapidly lose their virulence in culture. Transplanted into the trachea of rabbits or pigeons, they produce a pseudo-membrane and a severe, rapidly fatal, disease. The filtrate obtained from a pure culture of diphtheria bacilli contains a powerful toxin which, upon injection into animals, brings about a violent local reaction and later may lead to death with paralyses. Animals which have withstood such an injection contain in their blood a specific antitoxin which is capable of inhibiting the poisonous action of diphtheria bacilli. The diphtheria antitoxin of Behring is prepared from the blood serum of large animals which have received repeated injections of diphtheria toxin.

Diphtheria bacilli stain best with Lœffler's methylene blue, and are gram-positive. They are demonstrated by staining a bit of the pseudo-membrane removed from the pharynx, or by culture; an absolute diagnosis may be made only by the latter method. Neisser's polar body stain produces a characteristic picture. A specimen of an 8–20 hour blood serum culture is smeared upon a cover-glass and stained with a freshly prepared mixture of 2 parts of A with 1 part of B (A: methylene blue 0.1, absolute alcohol 1.0, distilled water 100.0, glacial acetic acid 5.0; B: crystal violet 0.1, absolute alcohol 1.0, distilled water 30.0). Wash with water and stain for 10–15 seconds with chrysoidin solution (chrysoidin 1.0, distilled water 300.0, dissolved while hot and filtered). The polar bodies then appear blue against a brownly-stained bacterial body.

Diphtheria bacilli may be cultured upon glycerine-agar or Lœffler's blood serum (3 parts blood serum, 1 part peptone broth, 2% glucose). This medium is prepared in Petri dishes or test-tubes. A portion of the membranes or a sterile swab, which has been rubbed over the membrane, is streaked upon the plate; after 12–24 hours incubation at 37° small grayish-white colonies appear in the region of the inoculation. In addition to the colonies of diphtheria bacilli there appear those of streptococci and other organisms of the throat. For

this reason it is advisable to make several cultures from the same swab to prevent too thick implantation. A negative result is only to be assumed after the examination of a large number of colonies and of smears from the cultures. The diphtheria bacilli are identified by their morphological characteristics. With the usual stains the bodies of the bacteria appear vacuolated. In the majority of cases the physician is not prepared to make the elaborate bacteriological examination himself. It is, however, advisable that he submit a throat culture, obtained with a sterile swab, to the nearest bacteriological institute. Such throat cultures should be taken before any disinfectant gargle or irrigation is prescribed.

Very similar to diphtheria bacilli are the organisms found in xerosis of the conjunctiva, and the pseudo-diphtheria bacilli which infest the mouth and nose. The genuine diphtheria organisms are distinguished, first in that they produce acid in litmus-neutrose-glucose broth, second that they kill guinea-pigs as the pseudo-diphtheria bacilli do not, third, pseudo-diphtheria bacilli show no polar bodies upon culture upon blood serum, and finally diphtheria bacilli grow upon alkaline glucose-agar anærobically whereas pseudo-diphtheria do not.

Diphtheria, after an **incubation** period of from 2–5 days, usually begins insidiously with tonsillitis, sore throat and gradually rising temperature, pallor of the face and anorexia. In the pharynx there appears a white membranous deposit which spreads from the tonsils upon the soft palate and fauces. Swelling of the regional lymph glands and, in severe cases, spreading of the membrane into the naso-pharynx and into the larynx, trachea and bronchi, sometimes causing suffocation. The susceptibility of an individual to diphtheria may be determined by the injection of a very dilute solution of toxin intracutaneously (Schick reaction, see page 323).

Sequelæ: Paralysis of accommodation, paralysis of the palate bringing about regurgitation through the nose, and generalized polyneuritis with pain, paralyses, anæsthesias, and abolition of reflexes.

In contrast with diphtheria, **angina tonsillaris** usually begins in a stormy fashion with high fever, red face, headache, sore throat, dysphagia, and painful swelling of the glands at the angle of the jaw. Upon the tonsils there develop numerous

yellow or yellowish-white points and deposits at the openings of tonsillar follicles which extend deep down into the lacunæ. Sometimes confluence of these deposits forms pseudo-membrane which, in contrast to the membrane of diphtheria, may be easily removed. In throat culture these cases show usually hæmolytic streptococci, more rarely pneumococci. The fever lasts from 4–7 days and falls by lysis.

Sequelæ: Peritonsillar abscess (quinsy) with localized swelling of the fauces on the infected side, causing difficulty in opening the mouth, terrific pain, and swelling of the lymph glands at the angle of the jaw. Unless drained such abscesses usually rupture through or near the tonsil between the 5th and 8th days. Acute hæmorrhagic nephritis, acute polyarthritis, otitis media, endocarditis.

Chronic infection of the tonsils causes pocket-like accumulations of pus deep in the crypts which may be pressed out in the form of white, caseous plugs through the lacunæ (chronic tonsillitis).

Bacillus fusiformis. In certain cases of tonsillitis, in many ways similar to diphtheria, there are found spirochætæ (Vincent's angina) and thick spindle-shaped bacilli. These are distinguished in the Giemsa stain by the presence of reddish granules in the blue cells; they may be cultivated only anærobically upon ascitic fluid-agar. Vincent's spirochætæ may be demonstrated by examination in the dark-field preparation.

Streptobacillus Ulcus molle (Ducrey-Unna). Very small, short bacilli with rounded ends which stain more deeply than the mid-portion. They may be cultivated upon blood agar; stain in smears with anilin dyes, best of all after 30–40 minutes in a solution of methylene blue and boric acid, and are gram-negative. They are found in the secretion of the soft chancre and in the pus of the complicating bubo.

Incubation period of the **soft chancre** 1–2 days (**in contrast** to the **hard chancre** of **syphilis** 14–21 days), followed by the formation of a phagydenic ulcer upon the glans or foreskin. Complications, purulent inflammation of the lymph glands. (Buboes.)

Influenza bacillus (Pfeiffer) (Fig. 104), very small rods which were isolated by Pfeiffer from the sputum, from pneu-

monic areas and from empyema in cases of influenza. The bacilli are ærobic and grow best at body temperature upon blood agar; the colonies appear as very small droplets. They do not grow upon the ordinary media. They stain well with Ziehl's solution, particularly if heated, and are gram-negative. In the early stages of influenza in previous epidemics these bacilli were found in enormous numbers in the sputum but in the last pandemic more rarely. The identification of this organism can be made with accuracy only in culture on hæmoglobin-containing media. Similar "hæmoglobinophilic" bacilli which, like the influenza bacilli, grow only on blood-containing media, have lately been described in other diseases, particularly in bronchitis and bronchopneumonia

FIG. 104.—Influenza bacilli. Pure culture.

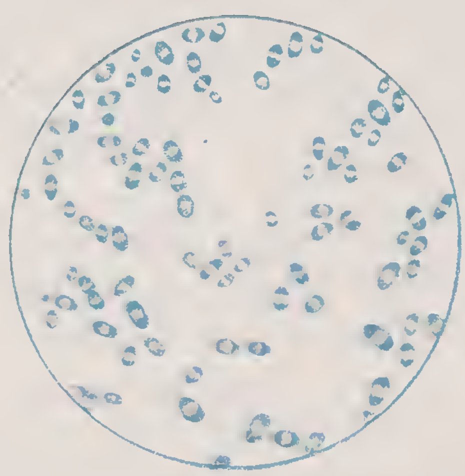


FIG. 105.—B. pestis. Pus from bubo.

but also in bronchiectasis and tuberculosis with cavitation. They are particularly common in children, e.g., in the sputum in whooping-cough. Their relation to influenza, and at the same time the etiological significance of the influenza bacillus, has recently been brought into question.

According to recent German and American studies grippe is caused by ultravisible virus which may pass through an unglazed clay filter (**filter passer**). This filterable virus has been shown by certain American authors to be a small bacillus-like organism (bacillus pneumosintes), which may be kept for months in glycerine and grows anærobically in culture; it is said to produce characteristic changes in rabbits. The American authors have succeeded in producing pulmonary emphysema and œdema with hæmorrhage and fever in the experimental animals (without, however, pneumonia) by the

injection of filtered nasal secretions from cases of influenza. Pneumonia, it is supposed, develops as a secondary complication in human influenza through infection with pneumococcus, streptococcus, or Pfeiffer bacillus. Pfeiffer still maintains the etiological significance of his bacillus which he was able to isolate from 76% of the cases of the epidemic of 1920-21.

In epidemic **grippe** after an **incubation period** of 1–3 days there develop rapidly rising temperature, backache, headache, and pain in the legs, usually associated with catarrh of the upper respiratory passages, and more rarely vomiting and diarrhœa. The fever lasts 3–7 days. Influenza is sometimes complicated with bronchopneumonia which has a tendency to progress to abscess-formation or empyema. Occasionally also sinusitis, otitis media, or, still more rarely, myocarditis may follow. Hæmorrhagic encephalitis and meningitis, polyneuritis, and neuralgia and nephritis sometimes appear as complications.

Also in the common cold and in catarrhal inflammations of the upper air passages Kruse, and recently American authors, have demonstrated an invisible virus which passes through a Birkfeldt filter. Transferred to monkeys it produces the same symptoms as in man. In the secretion of this so-called "cold," which is transmitted by contagion from person to person in the same household, and which usually has nothing to do with the effect of cold and wet, there can usually be identified many visible and cultivatable microorganisms (pneumococcus, catarrhal micrococcus, streptococcus, influenza bacillus).

Bacillus proteus, a medium sized rod that is actively motile, appears in various putrefactive processes. It is found, among other conditions, in the foul urine of pyelitis and cystitis.

Weil and Felix have cultivated a certain form of bacillus proteus (type X 19) from the urine of patient with typhus fever. This type is agglutinated consistently by the serum from typhus patients. Although B. proteus apparently has nothing to do with the etiology of typhus fever this agglutination reaction is to be regarded as of diagnostic significance. See also page 370.

Bacillus of the bubonic plague: **B. pestis,** (Fig. 105), short, thick bacillus with rounded ends, non-motile; found in the pulp of the swollen lymph glands in patients with plague, in the blood in large numbers in severe cases and near the end of the disease; also in the sputa of patients with the bronchitic and pneumonic form of the disease. Stains easily with all the basic anilin dyes; gram-negative. In the stained specimen there appears a characteristic polar staining. This bacillus shows a capsule with certain staining methods; grows easily upon all the usual bacteriological media at room or body temperature, best at 30–35° C.; does not liquefy gelatine. Infection takes place in man usually through superficial wounds in the skin or via the respiratory or digestive organs. The plague is primarily a disease of rats and other rodents and is presumably transmissible to man by fleas. The demonstration of the disease rests upon the discovery of the characteristic bacteria, and upon the production of the disease in rats or mice by the inoculation of material from a bubo, or of the pure culture. These organisms are agglutinated by the serum of immunized animals or of human beings convalescent from the disease.

The **plague** occurs in two forms: The **bubonic** and the **pneumonic.** The latter ensues, supposedly, when the bacilli are aspirated, e.g., by contact with a coughing individual with the pneumonic type (droplet infection) or from the dust of ships and granaries infested with rats. This form progresses as a malignant, hæmorrhagic pneumonia and is almost always fatal. The bubonic form brings about swelling, pain and purulent inflammation of the lymph glands in whose domain the infecting flea bite or skin injury has taken place, e.g., in the groin or axilla. From this primary bubo the disease spreads, accompanied by a high fever, to more distant lymph glands, or a blood infection ensues and therewith a generalized disease. A carbuncle-like lesion may also appear at the site of infection. **Incubation period 2–5 days.**

Tetanus bacillus (Fig. 106), motile rods, which, in old cultures, show a spore at one end producing a knob-like protrusion, like a drum-stick. They are found in tetanus in the pus of the infected wound but not elsewhere in the organism; in tetanus neonatorum they appear in the umbilicus. They are found also in cultivated earth and in the sweepings from the

street particularly when this contains remnants of horse manure; tetanus arises particularly in wounds which have been contaminated with such material. Tetanus bacilli may be cultured from such wounds or from the earth; they prove to be strictly anærobic, i.e., they thrive only in cultures from which air has been excluded, or in an atmosphere of pure hydrogen. In subcultures they rapidly lose their virulence. In the body and in culture they produce two forms of toxin, **tetanospasmin** and **tetanolysin** of which the first produces the symptoms of lock-jaw. Mice or guinea-pigs infected with pus or earth containing tetanus bacilli, or with the pure culture of the same, die of tetanus. In the serum of such animals as have been treated with sublethal doses of tetanus toxin there is

Fig. 106.—Tetanus bacilli.
Pure culture.

developed an efficacious antitoxin. These organisms stain with the usual anilin dyes and are gram-negative.

Tetanus (lock-jaw) begins with pain and stiffness about the infected wound and in the extremity involved, together with tonic spasm of the muscles. If it come to involve the head, the muscles of the mouth and eyes are drawn to a grin, the folds of the forehead and nose deepen and by the tetanic contraction of the jaw muscles the teeth are clenched so that the mouth cannot be opened. Upon almost any stimulation generalized, painful extension of the entire body may take place (opisthotonus); the spasms may involve the diaphragm. Often high fever with profuse sweats. **Incubation period 4–14 days,** seldom longer. The later the disease appears after the injury the better the prognosis. Mortality as high as 80%. For therapy, as well as for prophylaxis, antitetanus serum

should be injected, i.e., the serum of horses which have been rendered immune by repeated injections of tetanus toxin. [As a prophylactic measure the injection of tetanus "toxoid" is to be recommended. (Material is available at the office of the Board of Health in nearly every community.) Ed.]

The **bacillus of malignant œdema** (Koch), somewhat more slender than the anthrax bacillus, with rounded ends. These bacilli are found in cultivated earth (like the tetanus bacillus) and are strictly anærobic; they stain with all the anilin dyes, are gram-negative, and produce in man œdema and emphysema of the skin. They are to be isolated from the œdema fluid.

Gas bacillus (E. Frænkel) is found in cases of gas gangrene. Upon liver broth, and in the human tissues it rapidly forms gas. In contrast with malignant œdema and anthrax this organism is non-motile, gram-positive and forms no spores, but, on the other hand, is also strictly anærobic. In addition to Frænkel's bacillus certain other gas-producing, motile bacilli are met with in gas gangrene. Gas gangrene resulted in the war from such wounds as were contaminated with earth or mud. About the wound there develops œdema and crepitating vesicles which gradually burrow into the tissues and muscles, causing putrid disintegration. From the mouth of the wound is discharged a bloody, serous, foaming fluid. Temperature irregular, dyspnœa and symptoms of general intoxication; the infection is frequently fatal. A toxin may be demonstrated in the broth culture and an antitoxin prepared by injecting horses with such material.

Bacillus botulinus is a motile rod which stains with all anilin dyes and is gram-positive. It often carries a spore at one end, similar to the tetanus bacillus, and grows only anærobically. In culture, as well as in infected fish, meat or preserved vegetables, it develops a powerful toxin which acts particularly upon the nervous system. Infected preserves sometimes have a peculiar odor but are otherwise not conspicuously altered. Botulinus does not multiply in the human body and, in contrast with the paratyphoid bacillus, it causes no gastrointestinal symptoms and no fever; 24–36 hours after the ingestion of food infected with botulinus there begins a series of symptoms which are very suggestive of atropine

poisoning: Fixed, dilated pupils, paralysis of accomodation, diplopia, suppression of saliva with dry mouth, dysphagia, aphonia, urinary retention, finally disturbances of cardiac function, asphyxia, and in many cases death. Antitoxin available at local Board of Health in most cities.

Cholera vibrio (Koch) (Fig. 107). Short, very actively motile, bent rods (comma bacilli), which develop into spirilla-like forms. They thrive at room temperature upon gelatine, which they liquefy in a characteristic fashion (forming a funnel-like depression about the colony), and also in broth and peptone solution; they remain viable for a long time in water. If a peptone culture of these organisms be treated with sulphuric acid there develops a reddish-purple color due to

FIG. 107.—Vibrio cholera asiatica.
Pure culture.

the production by these bacteria of indol and nitric acid. This **"nitroso-indol-reaction"** appears not only with cholera vibrio but with certain other bacteria. Cholera vibrio stain best with concentrated aqueous fuchsin solution. They are found in the intestinal contents, and in the superficial layers of the diseased intestinal mucous membrane, but apparently do not penetrate deeper into the tissues of the body. In the **"rice-water stools"** of the cholera patient they are found in swarms, often in pure culture. Suggestive as their microscopic picture is, diagnosis should only be made by culture since there are often present in the stool other similar bacteria. A carefully packed specimen of the stool should be sent at once to the nearest bacteriological station. Dieudonné has described a medium which makes possible the elective cultivation of cholera vibrio from the stool. Equal parts of beef blood and normal potas-

sium hydroxide are mixed; this mixture is sterilized and 2 parts thereof are added to 7 parts of nutrient agar. Upon this strongly alkaline **"blood-alkali medium"** colon bacilli and the other intestinal bacteria will not grow whereas cholera vibrio appear to thrive. There are large numbers of cholera-like bacteria in our environment particularly in contaminated water, which are to be differentiated from cholera bacilli only with difficulty. In any suspected case stained preparations should be made from the fæces and rectal mucous membrane of the patient, cultures should be planted on gelatine and in peptone water.

The onset of **cholera** follows an **incubation period of 1–4 days** and is marked by vomiting and profuse diarrhœa; the stools soon lose their formed character and appear like rice-water mixed with small particles of mucus. There follow abdominal pains, tenesmus and fever; at the same time thirst, weakness; the eyes become sunken and the face drawn; aphonia (vox cholerica). In mild cases this condition may improve after the 1st or 2nd day but in severe cases it progresses with prostration, weakness and exhaustion, fall in temperature, cold sweats, cramps in the extremities, and small thready pulse. If the patient survive this, the condition may go on to the so-called "cholera typhoid" a protracted severe disease characterized by fever, delirium or coma and albuminuria. In the most severe cases death may result after a few hours, even before the occurrence of the diarrhœa. Mortality on the average about 50%.

Prophylactic inoculation is accomplished by two injections, at an interval of 8 days, of a pure culture killed by heat at 54°. The material for inoculation may be obtained from municipal or state departments of health.

Malta fever which is prevalent in the Mediterranean countries (and also sporadically in the United States) is caused by an extraordinarily small coccus (**micrococcus melitensis** of Bruce). This organism stains with all the anilin dyes, is gram-negative and grows best upon ascitic-fluid agar. It is found in the blood and splenic pulp of patients with the disease, and is agglutinated by the serum of convalescents. It is transmissible to animals, particularly to goats, and, in these animals, is found in the milk.

Malta fever begins after an **incubation period of 5–14 days** with headache, sleeplessness, vomiting and rapidly rising fever, which lasts for 1–3 weeks with morning remissions and profuse sweats, and then falls gradually. After several days or a week there is a relapse which may last, with afebrile intervals, for several weeks. In severe cases the disease is very similar to typhoid. The spleen and liver are often enlarged and the white blood count diminished. There is usually swelling and pain in several joints and not infrequently orchitis. Mortality about 2%.

Bacillus abortus (Bang) is very closely related to the bacillus melitensis, perhaps identical with it. It is found in the uterus and vaginal secretion of cows and may be transmitted among cattle and by them through contact to stable-hands, farmers, butchers, veterinaries, etc. In spite of its prevalence among cattle, epidemic infection with bacillus abortus has never been observed in man, although sporadic cases have occurred which were apparently ascribable to drinking raw milk. The disease has increased chiefly in dairy countries in the last years (Switzerland, Denmark, etc.); it also has been observed in Germany. It bears a great similarity to Malta fever; the onset is marked by exhaustion, loss of appetite, headache, neuralgia and recurrent fever. Characteristic of bacillus abortus infection is the fact that, despite high fever and protracted course, constitutional symptoms are relatively mild. The outstanding signs are enlargement of the spleen and liver, leukopænia—at first with preponderance of the myeloid elements, later with lymphocytosis—and pain and swelling of different joints. The disease may last for many months with recurrent fever. Severe complications or death occur seldom. Diagnosis by agglutination and complement fixation.

Sepsis (septicæmia, blood poisoning) is a generalized disease produced by the penetration of pathogenic micro-organisms, particularly of the pyogenic variety, into the blood and thence into the entire body. The generalized infection is usually distributed from a local focus, e.g., an infected uterus (puerperal sepsis), from an infected wound, otitis media, streptococcus angina, from the bile or urinary passages, (e.g., following pyelonephritis or gonorrhœa). In

infants sepsis may arise from the infected stump of the umbilical cord. Systemic infection may proceed from a local focus either through the lymph channels or through the blood stream, where it usually is carried by the venous blood. If the causative agent is demonstrable in the circulating blood the condition is spoken of as a **bacteræmia**; such a condition may be transient in many infectious diseases and does not always indicate true sepsis, e.g., in typhoid and pneumonia. In many cases of sepsis there develops an inflammatory reaction in the inner layers of the wall of the circulatory apparatus, e.g., thrombo-phlebitis in the veins, or endocarditis in the heart. When the causative agent, having penetrated into different organs (liver, lung, brain, muscle, etc.) produces abscesses therein, there results a condition usually accompanied by repeated chills and sudden rises in temperature (**pyæmia**). **Septicæmia** is accompanied by a high, irregular fever which may last for weeks. Splenomegaly is almost always present and, in the advanced stages of the disease, an hæmorrhagic nephritis. Occasionally there develops an hæmorrhagic exanthem or arthritis. Sepsis is very often fatal and recovery is to be expected only when the primary focus is removed in its early stages. The condition may be caused by various microörganisms, most frequently by streptococci. Infection with streptococcus viridans causes a chronic disease characterized by low fever, malignant endocarditis and anæmia and is usually fatal. Staphylococcus septicæmia is usually accompanied by chills (also pyuria, Ed.). Pneumococcus sepsis often follows middle ear infection; that with colon bacillus a pyogenic process in the gall-bladder or kidney; gonorrhœa is occasionally, though rarely complicated by gonococcus sepsis with endocarditis.

Acute polyarthritis, the so-called **acute rheumatic fever,** is in many ways similar to septicæmia. It often follows a primary infection in the tonsils, i.e., acute or chronic tonsillitis. Concerning its causative agent there is no unity of opinion since microörganisms are rarely found either in the blood or in the lesions upon the affected valves. However, in cases with endocarditis streptococci have been repeatedly demonstrated (Poynton and Paine, Wassermann, Small, Swift). Transfer of these streptococcus cultures to animals

does produce an arthritis. Other organisms have been isolated from cases of polyarthritis, e.g., staphylococci.

Polyarthritis is characterized by a high and often protracted fever and inflammation of the joints (synovitis), which usually involves several joints in turn. The affected joints are swollen and very painful. In about one-third of the cases the heart is involved by an endocarditis which usually attacks the mitral valve. In the end, there often develops chronic valvular disease and, not infrequently, pericarditis and myocarditis (Aschoff bodies) as well.

Pertussis—whooping-cough is a contagious disease transmitted by direct contact and not by a third person. It appears predominantly in childhood but occasionally in adults; in the latter it does not run its characteristic course but appears simply as a cough. Bordet and Gengou have found, in the sputa of patients with pertussis during the first two weeks a small, non-motile bacillus showing polar staining, which may be cultured upon blood agar. The fact that this organism is agglutinated only by the serum of convalescent pertussis patients argues strongly for its etiological significance. Injection of a pure culture into the respiratory passages of monkeys produces the disease.

Pertussis begins after an **incubation period of 3–8 days** with a low fever, weakness, anorexia, catarrh of the upper respiratory passages, and cough. In older children there sometimes appears a small ulcer upon the frenulum linguæ. The first catarrhal stage, which is to be differentiated only with difficulty from a common coryza, lasts about 1–2 weeks. The fever then falls and the second stage sets in with the paroxysms of coughing; once an hour, or more often, there begins suddenly violent coughing which persists until the expiratory volume is exhausted. Forced inspiration through the narrowed glottis produces the characteristic whooping noise. These attacks may be repeated until the child is blue in the face and paroxysms are usually terminated by retching or vomiting. These attacks are repeated one after another. The second stage usually persists for 4–6 weeks, but may last for months passing over gradually, with milder and milder seizures, into the third or catarrhal stage. The disease is apparently most contagious during the first week. Complications: Bronchitis, bronchopneumonia, rarely encephalitis.

Mumps (parotitis epidemica) is a contagious disease, caused by a filtrable virus. The infectious stage may last for several weeks. Following an **incubation period of 18–23 days** there begins a painful swelling of the parotid gland and its surrounding tissue, accompanied by fever, headache and malaise. After about a week the temperature falls gradually and the swelling disappears; purulent inflammation of the gland almost never occurs. Frequently, however, either at the same time or several days later and accompanied by a rise in temperature, the other parotid gland becomes involved and occasionally the submaxillary and sublingual salivary glands as well. Sequelæ: In adult men orchitis not infrequently develops, with a febrile reaction and sometimes atrophy of the testicles; occasionally meningismus, and more rarely pancreatitis.

Heine-Medin's disease (spastic spinal paralysis of infants) occurs most frequently in the form of **acute anterior poliomyelitis,** but sometimes as a transverse myelitis, and encephalitis or disease of the brain stem and medulla. It appears occasionally in adults but usually in children (infantile paralysis) as an infectious disease occurring in epidemics. **Incubation period 2–5 days.** Flexner and Noguchi have cultivated a microörganism from such cases upon ascitic fluid under anærobic conditions. It is so small that it passes through a clay filter and is microscopically visible only in the form of small spherical bodies. The ætiological significance of this microörganism has recently been questioned. However, the causative agent of poliomyelitis may be transmitted by inoculation of the nasal secretion or of the spinal cord from infected cases to monkeys and other animals, in which it produces a similar spinal paralysis.

Among the diseases due to **filter passers** (filterable viruses) belong in addition to those already named yellow fever, Pappataci fever, dengue fever, and probably the common cold, rabies and small-pox. In all these diseases the causative agent has yet to be demonstrated but, in the majority, the mode of transmission is understood.

Encephalitis lethargica commences with several days of fever and headache and advances with increasing drowsiness and stupor, stiffness, spasticity of the extremities and fixed,

expressionless facies. Ocular palsy with diplopia and in many cases nystagmus; in children and young adults choreic twitching, and other indications of motor irritation; occasionally cerebral or spinal paralyses. Lumbar puncture gives no characteristic findings. The disease often lasts for many weeks and is not infrequently fatal. If the patient recovers there persists generalized stiffness and immobility of the facial musculature, and sleeplessness; occasionally psychic disturbances, rarely dementia. Anatomically there are found small foci of encephalitis in the region of the aqueduct of Sylvius and the 3rd ventricle and particularly in the basal ganglia. The disease appears in epidemics, which have been associated chronologically with those of influenza. In human beings the disease proceeds presumably from the nasopharynx and possibly after contact with carriers. Doerr succeeded in producing encephalitis in rabbits by the corneal inoculation of the contents of herpes vesicles. At the same time the identity of the herpes virus and that of human epidemic encephalitis is still far from proven.

Encephalitis, characterized by stupor, lethargy and cranial-nerve palsies, and similar in many respects to encephalitis lethargica may sometimes follow epidemic influenza, measles, small-pox, and, unfortunately, vaccination.

Pappataci fever is endemic about the Mediterranean and appears during the warmer seasons. It is transmitted by a flea which is so small that it may penetrate the meshes of the ordinary mosquito netting.

After an **incubation period of 3–8 days** the disease begins with a high fever, violent headache, and pain in the back and eyes. Conjunctivæ injected, photophobia, herpes labialis, exanthem similar to that of measles or scarlatina, slightly positive Diazo-reaction; tenderness of the musculature over the whole body. The fever lasts 3–5 days and then falls by lysis; the pulse rate is sometimes slow, sometimes very rapid. During convalescence weakness and psychic depression, and polyuria.

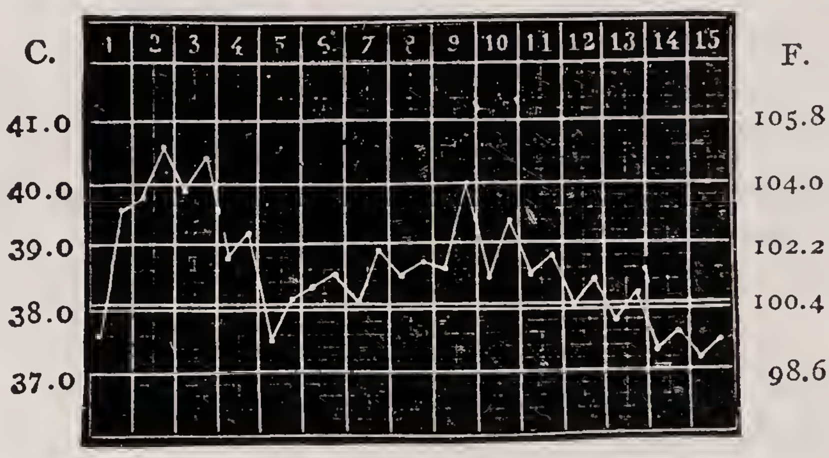
Dengue fever is a disease of the tropics and subtropical countries occurring usually during the summer. It is transmitted by a type of mosquito, culex fatigans.

An **incubation period of about 3 days** is followed by fever, headache and severe pain in the joints, particularly the hips. The joints are often swollen and reddened and the muscles painful and stiff; the patients feel very ill and every movement is extremely painful. After 1 or 2 days the temperature falls, to rise again on the 4th or 5th day, coincidentally with the eruption upon the hands, arms, breast and back of a macular rash composed of flecks a few mm. in diameter. On the 7th day there occurs the crisis, followed by a rapid convalescence.

Small-pox (variola) is transmitted by direct contact from person to person or through a 3rd individual e.g., the physician. The causative agent is very resistant and may remain actively viable for a long time in clothing, etc. It may also be carried through the air. The causative agent is unknown. Inoculation of material from a small-pox pustule into a small cut in the cornea of the rabbit causes, within the next two days, a grayish clouding. Upon microscopic examination there appear in the corneal epithelium round structures which stain dark blue with iron hæmotoxylin, the so-called Guarneri's bodies. These structures are also present following the corneal inoculation with vaccine lymph but not after the injection of the contents of varicella vesicles. Guarneri's bodies are specific for small-pox and important in the differential diagnosis. Paschen has demonstrated in the small-pox pustules, small round bodies which pass Berkefeld filter. In how far the Guarneri's bodies or the structures described by Paschen, are identical with the causative agent of small-pox, is still uncertain. Noguchi has cultured from vaccinia pustules very small microörganisms which may be cultivated in the testes of the rabbit and which, upon transmission to man, produce genuine variola pustules.

Variola begins acutely after an **incubation period of 8–12 days** with chill, headache and characteristic severe pain in the back. The temperature remains high for about 3 days during which time there sometimes develops the so-called prodromal exanthem, a scarlatina-form or rubelli-form reddening over the abdomen, upper arms and axillæ or, more rarely, over the entire body. If this initial exanthem be

hæmorrhagic (purpura variolosa), the disease is almost always fatal (black-pox). On the 3rd to the 5th day the temperature tends to fall and therewith begins the eruption of the true pox exanthem which appears primarily over the face, and the hands and feet, including palms and soles, but may also be distributed over the entire body as well as upon the mucous membrane of the mouth and the eyes. There form firm, red nodules, which upon palpation feel like granules and which rapidly develop into vesicles with a central depression and a reddened margin. The contents of the vesicle quickly dry in mild cases; in more severe cases become purulent or hæmorrhagic. With the appearance of this exanthem there sets in a second period of fever which is



(1) Prodromata. (2) Eruption. (3) Pus formation. (4) Desiccation.
FIG. 108.—Temperature chart in variola.

at first low, rises gradually for about 9 days, and after several days fastigium falls by lysis (stage of desiccation). On about the 16th day the crusts exfoliate and this is completed in about a week; during this time the patient is particularly infectious. This process leads to scar formation, particularly about the face.

Varioloid is the term given to a case of small-pox which develops in a patient previously vaccinated (with a positive result). The symptoms are in general much more mild and the vesicles do not tend to become purulent. As a result scar formation is much more rare.

Prophylactic vaccination is accomplished by the production of a localized lesion, without a generalized exanthem, by the inoculation of cow-pox lymph. At the first vaccination there develop, after 3 or 4 days, at the site of the inoculation, small vesicles which increase in size up to the 7th day. The

contents then become purulent and about the lesions there is an area of necrosis and inflammation. On the 8th to the 9th day the regional lymph glands become swollen and the temperature rises. From the 10th day on the pustules tend to dry up, the crust falls off after 3 to 4 weeks leaving a scar. Vaccination confers immunity for about 10 years. Revaccination produces either no vesicle or one which develops more rapidly and runs a milder course without necrosis (**accelerated reaction**).

Chicken-pox (varicella) bears no relation to small-pox: Vaccination with cow-pox serum does not protect against varicella and an attack of varicella confers no immunity against small-pox. In an individual with varicella small-

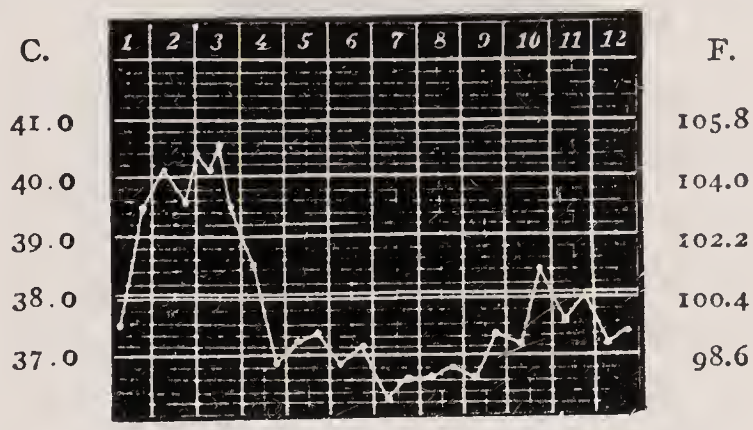


FIG. 109.—Temperature chart in varioloid.

pox vaccination may give a positive result. Causative agent unknown.

Incubation period 14–21 days, no prodromata. With a mild febrile reaction there begins an eruption of vesicles on the 1st day of the disease and these appear in several crops during the next few days over the face, body and extremities, as well as upon the mucous membrane of the mouth; they dry up again within 4–6 days.

Scarlatina (scarlet fever) is transmitted by direct contact or sometimes by a third person, by clothing or utensils.

Incubation period usually 4–7 days. The disease begins suddenly with chills, vomiting and sudden rise in temperature. On the 1st day there is a bright red angina, often with patches of white exudate and swelling of the glands at the angles of the jaw. The tongue, which is at first white and coated, later develops swelling of the papilli (**strawberry**

tongue). On the 2nd day of the disease a rash appears upon the neck, chest and back, which during the next few days gradually spreads over the remainder of the body and outward along the extremities: Small scarlet-red points which are confluent. Over the face there is diffuse reddening, which is characteristically absent, however, about the mouth and chin (circumoral pallor). With the diffusion of the exanthem the temperature rises, to fall, however, by lysis as the rash fades toward the end of the first week. During the next two weeks the superficial layers of the skin are exfoliated, sometimes in sheets. At the height of the disease there is a leucocytosis often with increase of the eosinophilic leucocytes. **Complications:** Severe and sometimes necrotic angina, cervical adenitis, endocarditis, arthritis, severe and destructive

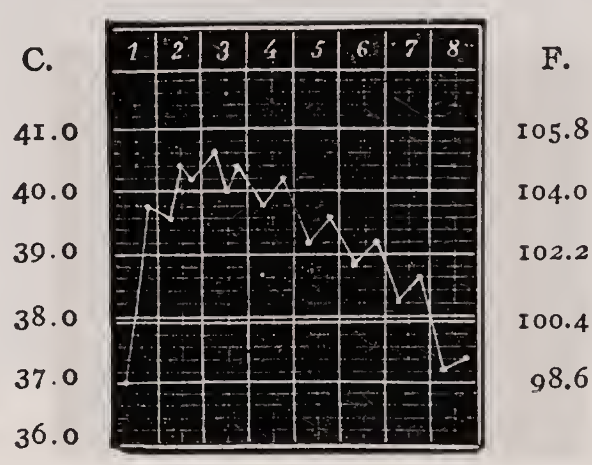


FIG. 110.—Temperature chart in scarlatina.

otitis media; in the complications there is usually a mixed infection but streptococci play a prominent part. Among the sequelæ hæmorrhagic glomerulonephritis is most serious; this tends to make its appearance during the 3rd or 4th week of the disease.

The injection of convalescent serum early in the disease seems to bring about a milder course. If convalescent serum or that of a normal individual be injected into the skin in an area involved by the scarlatina exanthem, the rash disappears for a small distance about the point of injection (Schultz-Charlton phenomenon). Recently the ætiology of scarlet fever has been assigned by Dochez and Dick to a streptococcus which is agglutinated by scarlatina serum in great dilution. It also forms a toxin against which there may be developed an effective antitoxic serum. Similar to the Schick

test for diphtheria, the Dick test may be used to demonstrate the susceptibility of an individual to scarlet fever: The intracutaneous injection of 0.1 c.c. of a 1/1000 dilution (saline) of the toxin of the scarlatina streptococcus, 1 part in 20 of physiological salt solution, produces a characteristic skin reaction, (a circumscribed area of redness and infiltration from 1–3 cm. in diameter), in individuals susceptible to the disease, after 6–18 hours.

Measles (morbilli) is transmitted by direct contact, presumably not by a 3rd person. The patient is infectious during the incubation period but not during convalescence. The causative agent is unknown, but is apparently present in the blood and in all secretions. **Incubation period 10–14**

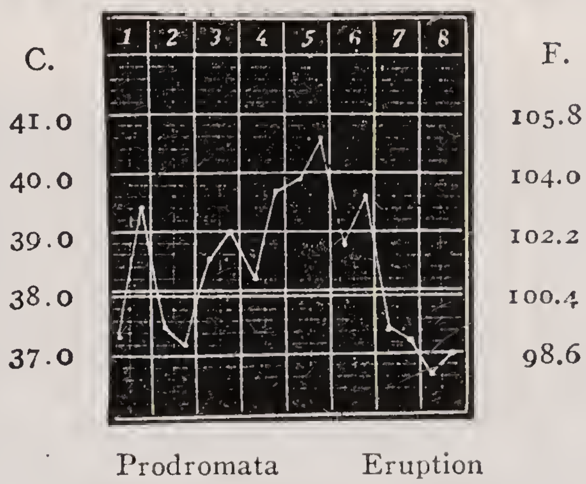


FIG. 111.—Temperature chart in measles.

days. The disease begins suddenly, sometimes with a chill, relatively high fever, coryza, cough, bronchitis, conjunctivitis and photophobia. On the 1st and 2nd days there appear small whitish flecks upon the inner surface of the lips and buccal mucous membrane; these **Koplik** spots are diagnostic. On the 2nd or 3rd day the temperature falls somewhat and the exanthem appears as bluish-red macules which soon become confluent; the rash begins on the face and in the course of the next 2 or 3 days, spreads over the back and extremities. Hand in hand with this the temperature rises, reaching the maximum on the 4th or 5th day, to fall rapidly after the 5th to the 7th day. Bran-like exfoliation follows and may last for 2 weeks. At the height of the disease there is a leukopænia. Complications are very frequently due to pneumococci: Bronchitis, bronchiolitis, broncho-pneumonia,

laryngitis and otitis media, occasionally gastro-enteritis. Prophylactic treatment with the serum of patients convalescent from measles is apparently effective in bringing about a shorter and milder course.

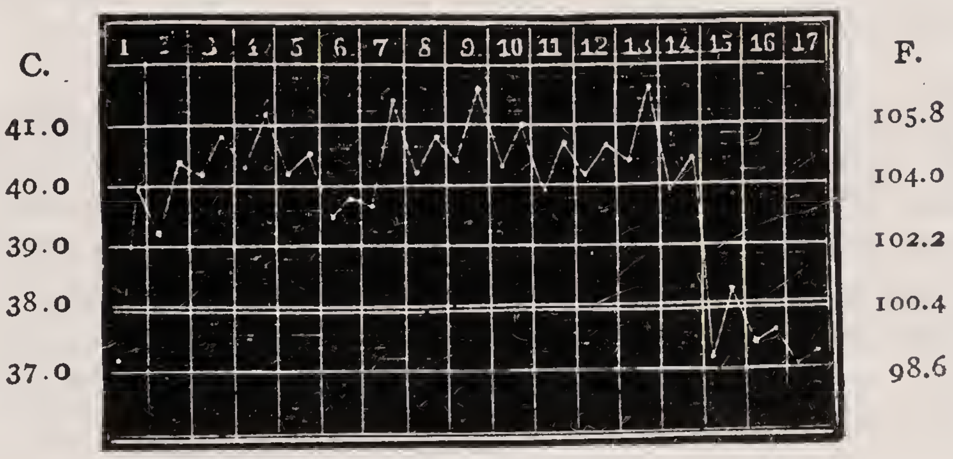
Rubella (German measles) is in reality unrelated to measles. **Incubation period usually 18 days.** With a mild fever there develop on the 1st day of the disease isolated reddish spots which never become confluent; these appear on the face and upper portion of the trunk. The rash fades rapidly with fall in temperature. No bronchitis, occasionally swelling of the lymph glands.

Fourth disease of Duke and Filatoff. This is a mild disease characterized by an exanthem with low-grade fever which begins after an **incubation period of 2–3 weeks** without prodromata, with the appearance of a scarlatina-form erythema. This diffuse eruption spreads over the entire body during the 1st day and, unlike scarlatina, does not omit the region about the mouth; mild fever for 1–3 days. Occasionally other morbilli-form exanthemata may appear (erythema infectiosum).

Typhus exanthematicus. This disease is transmitted by the body louse in whose blood or body the organism apparently develops. Such a louse having sucked blood from a patient with typhus may transmit the disease by its bite to another human being only after 5–7 days. Ricketts and von Prowazek found, in the intestine of the body louse infected with typhus, a small bacterium-like body which was absent from the control lice. These bodies are neither to be identified exactly with bacteria nor with protozoa. Whether or not this Rickettsia-Prowazeki is to be regarded as the causative agent of typhus fever is not proven, but its demonstration in lice infesting suspicious patients is of diagnostic significance. Also of diagnostic value is the fact that the blood of patients with typhus agglutinates a certain proteus-like strain of bacteria (proteus X19) which was isolated by Weil and Felix from the urine of typhus patients. This strain of bacteria is not, on the other hand, agglutinated by the serum of normal individuals or of patients suffering from diseases other than typhus. The causative agent of the disease is apparently present in the blood of typhus patients well into

the convalescence; the injection of blood serum, obtained from convalescent patients and heated to 52° C., into normal individuals exercises a certain protective reaction.

Typhus fever has an **incubation period of 4–14 days** and occasionally **21 days.** The onset is extremely rapid with prostration, headache, chill and rapidly rising temperature which reaches its maximum in 1–3 days. From this point on the temperature persists for 10–14 days with occasional remissions after the end of the 1st week. Rapid fall in temperature in the course of 2–4 days is observed in certain cases coincident with the development of myocardial failure. Death is usually due to circulatory insufficiency. At the beginning of the disease the conjunctivæ become injected and there develops a catarrhal inflammation of the upper respiratory passages, and bronchitis. The patient is often disturbed



(1) Eruption
FIG. 112.—Temperature chart in Typhus exanthematicus.

or delirious. Pulse rate from the beginning very rapid. In contrast to that in typhoid fever the blood shows a high leucocytosis. Diazo-reaction positive. On the 3rd–5th day appears the exanthem, which begins about the shoulders and spreads over the entire body including the forehead, palms and soles and occasionally the buccal mucous membrane. It, at first, resembles the roseola of typhoid, but the spots soon become dark or livid, similar to those of secondary syphilis. Finally, they may become hæmorrhagic as in purpura, and there may also appear bluish hæmorrhages in the deeper layers of the skin. The rash becomes more pronounced upon compression of the vessels, particularly in the extremities. Following the fall in temperature there is a bran-like exfoliation; and during this period the upper layers of the skin may

be rubbed off in sheets. Complications: gangrene of the extremities, peripheral neuritis with paralyses.

Five-day fever was frequently observed among the troops in South Russia and Rumania. **Incubation period 20–24 days.** Transmission by the body louse. The disease begins after a short period of malaise with headache, chill and rapidly rising temperature, and pain in the legs, particularly in the calves. After 1 or 2 days the temperature falls to normal and general well-being returns. On the 5th day the fever and symptoms return and this course is repeated 2 or 3 times with 5-day intervals. The spleen is enlarged, the liver swollen; leucocytosis with myelocytes. Diazo-reaction negative. In other cases the disease is characterized by fever of several days' duration and is similar to a mild attack of typhus. The pain in the calves may persist for some time during convalescence. As causative agent both a spirochæte and a Rickettsia-like body have been described.

Rabies (hydrophobia) is transmitted almost exclusively by the bite of a rabies-infected dog. After an **incubation period of from 2 weeks to several months** the disease begins with prostration or with a nervous excitement, often with paræsthesia at the site of injury, mild temperature reaction, headache and sleeplessness. After 1 or 2 days dysphagia may set in, due to cramps of the pharyngeal and œsophageal musculature and sometimes of the larynx upon any attempt at swallowing. The patient, therefore, in spite of severe thirst, avoids drinking since any attempt at swallowing brings on frightful cramps. These spasms may later spread to involve the muscles of the back and extremities. After several days asphyxia develops and leads rapidly to death.

The causative agent is unknown but is apparently a filter-passer. Infectious material is found in the saliva of the affected animal and above all in the central nervous system. In the cerebral ganglion cells small intracellular bodies (Negri bodies) may be demonstrated by Giemsa's method. The disease may be transmitted to rabbits by the introduction of macerated brain tissue from affected animals into the subdural space; this procedure is of diagnostic significance. Pasteur discovered that the virus becomes attenuated by drying the spinal cord of diseased animals; an emulsion of such dried material, injected in increasing doses into an infected human being, serves to prevent the outbreak of the

disease. Such a procedure should be followed in any case of bite by a suspected dog. Material for inoculation is obtainable from all State and City Health Departments.

Yellow Fever is endemic in the countries about the Gulf of Mexico, in South America and West Africa, and sometimes occurs sporadically in the coast cities of southern Europe. The causative agent is demonstrable in the blood of the patient and apparently belongs to the group of filtrable viruses. The disease is transmitted by the bite of a mosquito (stegomyia fasciata). The mosquito is infected by the blood of a yellow fever patient only during the first three days of the disease. The virus apparently matures in the body of the mosquito during a period of about twelve days, after which this insect may transmit the disease by biting another person. The bite of the insect is apparently infectious for weeks.

Yellow Fever begins after an **incubation period of 3–5 days,** with chill, high fever, acceleration of the pulse, pain in the head and limbs and especially in the loins. Conjunctiva injected. After a febrile period of 2–4 days the temperature sinks to normal. It soon rises again and jaundice makes its appearance. The liver is very sensitive to pressure, the urine scanty, rich in bile pigment and casts; bloody vomitus and very bloody stools, blood on the gums, delirium. In favorable cases the fever drops gradually at the end of the first week and the patient recovers slowly, mortality 30–90%.

(**Tularemia** is a disease of rodents, particularly of rabbits, caused by B. tularense. It is transmissible to man by direct contact with the flesh of an infected animal or as a result of the bite of certain ticks or flies. The causative agent, a short, gram-negative, non-motile rod does not grow upon ordinary media but may be cultivated upon blood-glucose agar to which cystine has been added. B. tularense is regularly agglutinated by the serum of patients suffering from the disease after the first week. Five c.c. of blood may be submitted for this purpose to the Hygienic Laboratory in Washington.

(After an **incubation period of 1–7 days** the disease begins suddenly with malaise, fever and prostration. In the most common, the ulcero-glandular type, painful enlargement of

regional lymph-nodes follows within 48 hours. Suppuration frequently ensues. The fever usually remains high for 2--3 weeks and then gradually subsides. During the active stage of the disease there is a moderate leucocytosis. In a small proportion of instances the disease may pursue an atypical course without conspicuous glandular manifestations. In such cases the agglutination test alone may establish the diagnosis. Ed.)

SUMMARY OF INCUBATION PERIODS OF INFECTIOUS DISEASES

	Days	
Soft chancre	1– 2	
Influenza	1– 3	
Anthrax	1– 3	
Erysipelas (eruption on 1st-2nd day of disease)	1– 3	
Cholera	1– 4	
Epidemic meningitis	1– 4	
Gonorrhœa	2– 3	
Heine-Medin's disease (Infantile paralysis)	2– 5?	
Diphtheria	2– 5	
Plague	2– 5	
Tularemia	1– 7	
Scarlatina (eruption on 2nd day of disease)	2– 8	usually 4–7
Bacillary dysentery	2– 7	
Dengue fever	3	
Yellow fever	3– 5	
Glanders	3– 5	
Pertussis	3– 8	
Pappataci fever	3– 8	
Erythema infectiosum and fourth disease (eruption on 1st day of disease)	14–21	
Tetanus	4–14	rarely longer
Typhus fever (eruption on 3rd-5th day of disease)	4–14	rarely 21
Relapsing fever	7–14	
Malta fever	6	
Typhoid fever (roseola at beginning of 2nd week)	7–21	
Malaria	7–21	
Small-pox (eruption on 4th day of disease)	8–12	
Measles, rubella (eruption on 3rd-4th day of disease)	8–14	
Sleeping sickness	10 ?	
Varicella (vesicles appear on 1st day)	14–21	
Rubeola (eruption on 1st day)	16–20	usually 18
Mumps (parotid swelling on 1st day)	12–21	
Syphilis I (from infection to appearance of hard chancre)	14–21	
Syphilis II (from appearance of chancre to secondary eruption)	21–50	
Rabies	14 days–several months	
Five-day fever	20–24	
Amœbic dysentery	21–24	

CHAPTER VIII

NERVOUS SYSTEM

THE CLINICALLY MOST IMPORTANT FEATURES OF THE ANATOMY OF THE NERVOUS SYSTEM

Introduction

The nervous system is built up of ganglion cells and nerve fibers, and of interstitial tissue, which in the brain and cord consists principally of glia. Including the glia, these tissues all develop from the ectoderm. In case of degeneration or inflammation in the central nervous system the glial cells proliferate. The result of this hyperplasia is a scar replacing the nervous tissue which has been destroyed, e.g., in multiple sclerosis, encephalitis or tabes.

The ganglion cell with its nerve fibers is regarded as a unit, the **neurone,** although it has been demonstrated that the fine fibers of the axis cylinder of one neurone may pass to the cell body of another. Among the nerve fibers extending out from a ganglion cell are distinguished, (1) the axis cylinder, which often may be very long and in its course give off numerous branches, so-called "collaterals," and (2) one or more dendrites, which have many branches, and which establish connection with other neurones. The **motor unit** consists of two neurones; (1) a **central,** which arises from a ganglion cell in the anterior central convolution and which passes through the pyramids of the medulla and the lateral columns of the cord to reach the anterior horn, and (2) a **peripheral** neurone, which has its origin in the motor ganglion cells in the anterior horn (or in a motor nucleus of the medulla) and includes the peripheral motor nerve fiber as well as its branches to the muscle fibers and the end plates. In addition to this path for voluntary movement there exists another, philogenetically older, motor tract which arises in the globus pallidus of the lenticular nucleus, passes to the red nucleus and thence through the medulla to the spinal cord. The **sensory unit** consists of a **peripheral** neurone

whose ganglion cells lie in the posterior root ganglion. From these cells one fiber passes as a sensory nerve to the periphery, to the skin or to various end organs, and the other, central, branch passes into the cord in the posterior root and ends about a ganglion cell in the posterior horn, or passes upward uncrossed in the posterior column to the sensory nuclei in the medulla. From the medulla the sensory paths pass in the lemniscus to the optic thalamus and from here to the parietal cortex.

If a ganglion cell is destroyed the nerve fibers arising from it degenerate. If an axis cylinder is severed from its ganglion cell the peripheral segment degenerates completely. If a **peripheral nerve** is severed or injured in any fashion **complete regeneration is possible; destruction of any portion of the central nervous system (brain or cord) is, however, never followed by regeneration.**

The meninges and the blood vessels of the central nervous system develop from mesoderm. Between the pia mater and the pia arachnoid lies the subarachnoid space, which in certain places enlarges to form the so-called cisterns, e.g., cisterna magna between the cerebellum and the medulla. Free communication exists between the subarachnoid space of the brain, the cerebral ventricles and the subarachnoid space surrounding the spinal cord. These spaces are filled with the cerebrospinal fluid, a water-clear, almost protein-free fluid containing very few cells (4–6). (See page 240.) With any form of meningitis, acute or chronic, the cerebrospinal fluid becomes more or less cloudy, its cell content rises and its protein content is increased.

The arteries of the brain are formed by branches from the internal carotid arteries on the one hand, and the vertebral arteries on the other, which join at the upper end of the medulla to form the Arteria basilaris. From the latter spring branches to the medulla, pons and cerebellum, as well as the Arteria cerebralis posterior, which supplies the occipital lobe and the under surface of the temporal lobe. From the carotid artery there arise the Arteria cerebralis anterior, supplying the ventral surface and the tip of the frontal lobe, and the Arteria cerebralis media, which supplies the basal ganglia, the internal capsule and the entire lateral aspect of

the cerebrum. The arterial vessels course beneath the pia and from them branches penetrate into the cortex or parenchyma.

In contrast with those elsewhere in the body the veins in the central nervous system do not course with the arteries but collect as large venous sinuses enclosed in the dura and emptying through the jugular foramen into the jugular vein. The venous blood from the interior of the brain is drained through the Vena magna into the Sinus rectus of the tentorium. Compression of this vein may cause congestion in the cerebral hemispheres or increase in the pressure of the fluid in the cerebral ventricles (Internal hydrocephalus).

The internal architecture of the several cortical regions varies; it is particularly developed in the region of the Fissure Rolandi. The anterior central convolutions contain large pyramidal-shaped ganglion cells from which axis cylinders pass downward through the internal capsule and the pyramidal tracts to the spinal cord, providing innervation for conscious movements. In the posterior central convolution, on the other hand, these pyramidal cells are wanting; in their place there are collections of spindle-shaped ganglion cells, the function of which is apparently associated with sensation. Such granular structure is particularly apparent in the region of the Fissura calcarina in the occipital lobe, in the so-called visual cortex. It is, therefore, to be assumed that the cerebral areas of granular structure receive centripetal sensory impulses, in contrast with those containing pyramidal cells from which are discharged centrifugal motor impulses.

The so-called psycho-motor region of the cortex is composed of the anterior central convolutions and the lobus paracentralis upon the median surface. The center for innervation of the leg lies in the latter and in the upper third of the anterior central convolution, that for the arm in the middle third, and the centers for the face, larynx and tongue in the lower third. From these motor cortical areas pass impulses which serve to innervate muscle groups, the coordinate contraction of which, together with inhibition of their antagonists, makes possible coordinated, purposeful movements, e.g., raising the arm, clasping the hand, and writing.

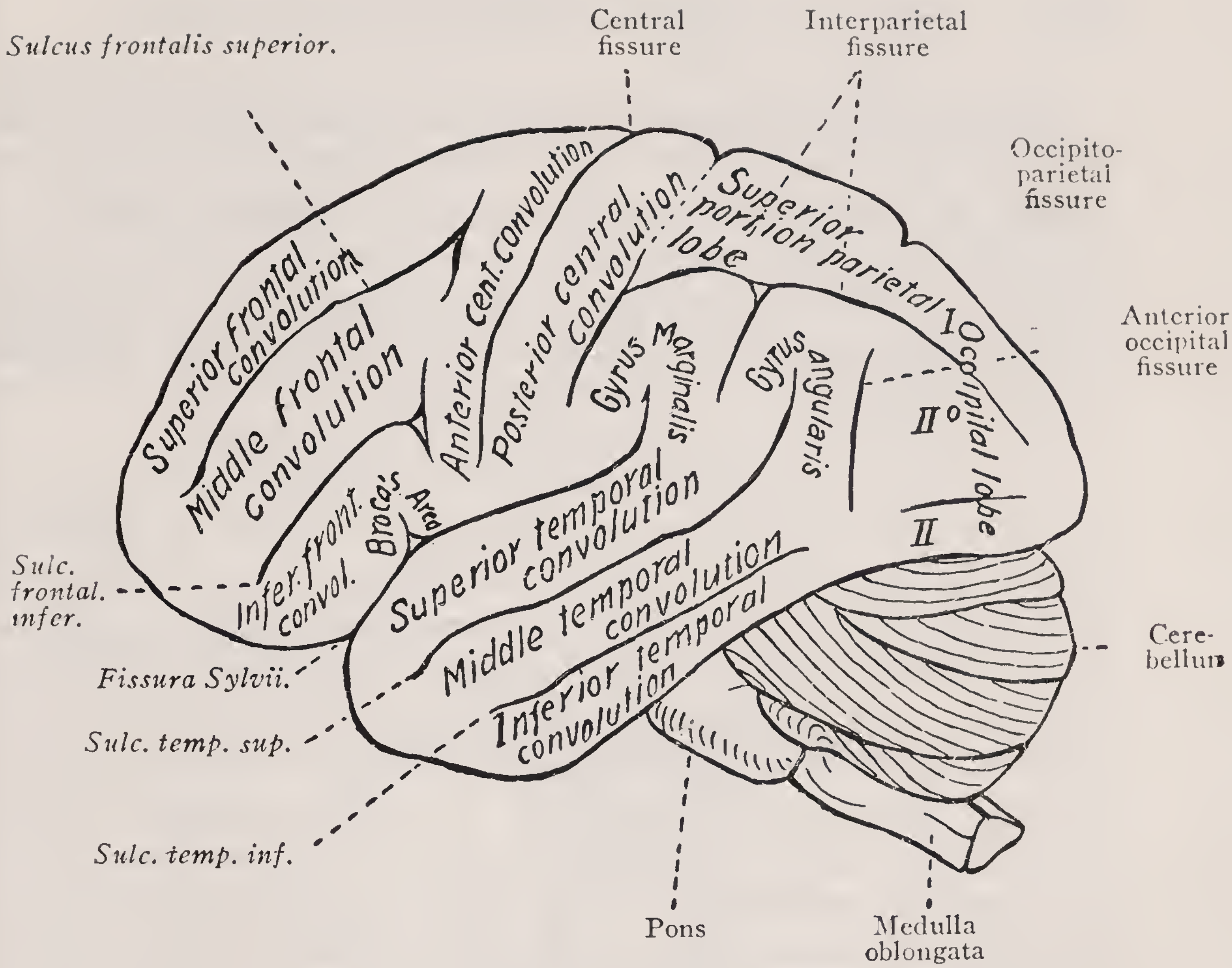


FIG. 113.—Lateral aspect of the brain.

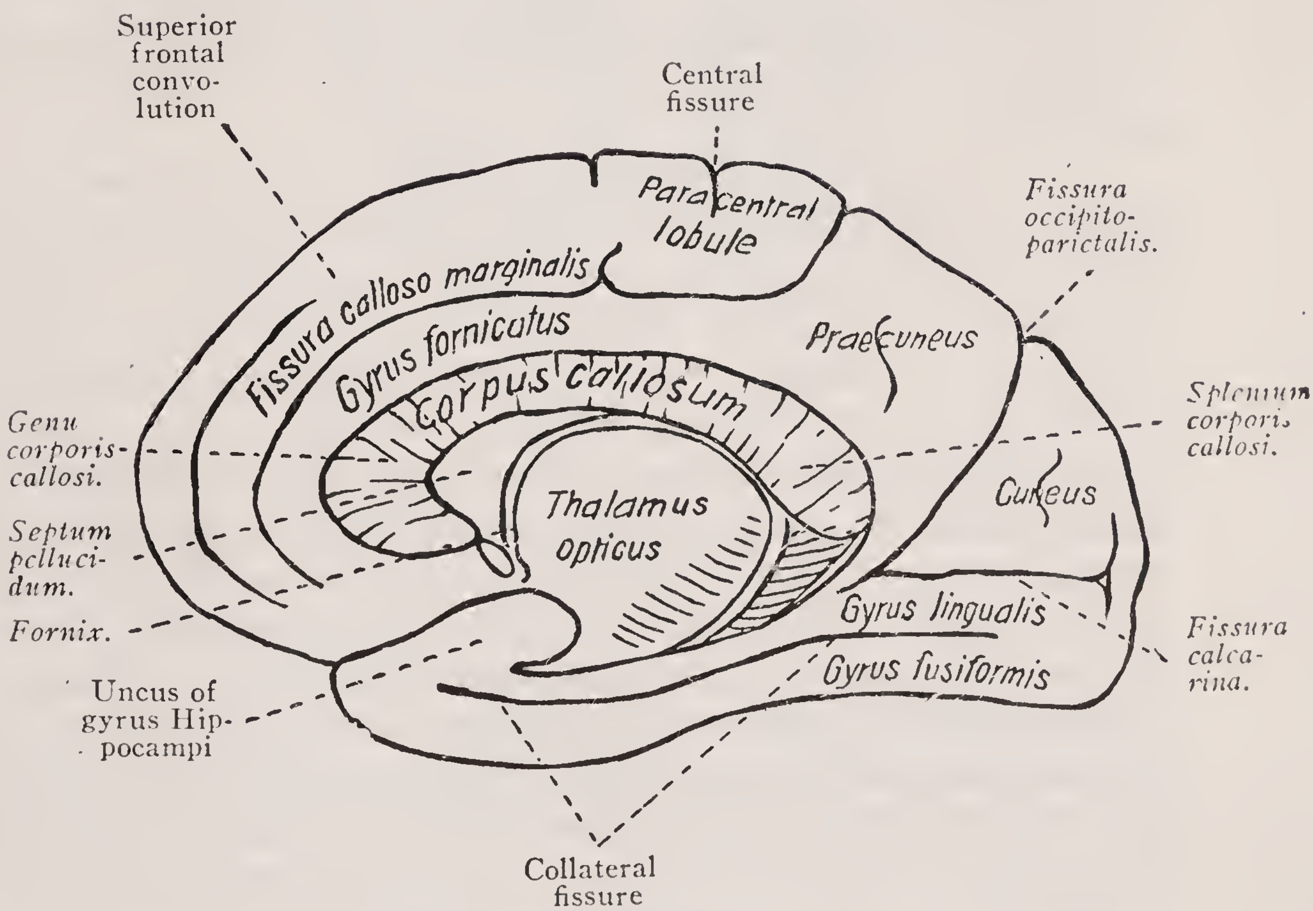


FIG. 114.—Median aspect of the brain.

Since, in the cerebral cortex, the motor centers of the various muscular groups are isolated from one another a **lesion in the cortex** produces usually a **monoplegia,** i.e., paralysis of a single extremity or muscle group alone; such lesions are often accompanied by paroxysmal convulsions (**Jacksonian epilepsy**). **Lesions of the internal capsule** usually bring about a **total hemiplegia** since here all the motor tracts are packed together in a narrow space.

The internal capsule and the adjacent region, particularly the lenticular nucleus, is not infrequently injured by **hæmorrhage** (apoplexy); the result is hemiplegia. In addition to hæmorrhage such hemiplegias are sometimes caused by vascular occlusion which produces an area of softening. Vascular occlusion may result from localized narrowing and thrombosis of the arteries with arteriosclerosis or syphilis (autochthonous vascular occlusion), or from an embolus arising from a heart valve, the seat of endocarditis. If vascular occlusion develop gradually, or if it involve only a small artery, loss of consciousness may not follow. Hemiplegia in young individuals is usually due to syphilitic disease of the vessels, or to emboli as a result of cardiac disease. Cerebral hæmorrhage and autochthonous arterial narrowing or occlusion are usually due to arteriosclerosis and commonly appear only late in life.

To the posterior central convolution there pass sensory impulses from the entire opposite side of the body, not only from the skin but also from the muscles and joints, i.e., deep sensibility. The sensory cortical areas in which the various regions of the body are represented stand in close anatomical relationship to the corresponding motor areas lying anterior to the central convolution. Thus, from above downward, are arranged the sensory areas corresponding to the legs, the trunk, arms and hands, the face and the tongue. The sensory and motor cortical areas are abundantly connected by fibers, so that, apparently, every movement is under continuous guidance and control of the sensory cortex. Lesions in the parietal lobe, particularly in the region of the Gyrus marginalis lead to disturbances of touch and particularly to loss of kinæsthetic function. Patients so affected are unable to recognize by touch (with their eyes closed) objects with which

they were previously familiar, e.g., a watch, spoon or a coin. Such **astereognosis** may sometimes affect only one or two fingers or one hand.

Sensory impulses from the entire body are conducted to the posterior central convolutions in the parietal lobes from the spinal cord and medulla by way of the median lemnisci and the lateral and ventral nuclei of the thalamus.

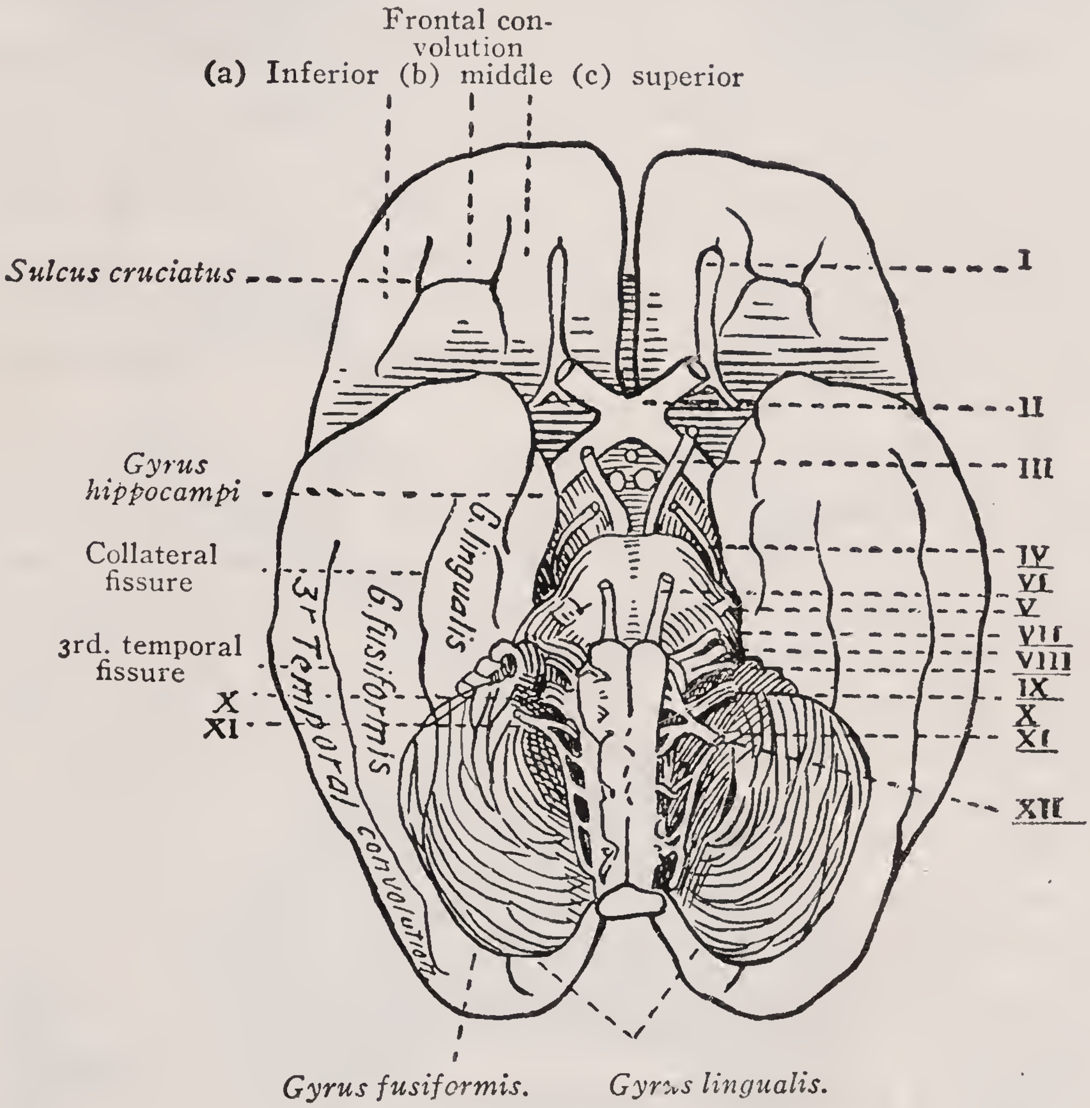


FIG. 115.—The base of the brain.

Near the lower end of the Island of Reil lies Heschl's gyrus (the transverse temporal convolution) which passes from the lower portion of the parietal lobe to the upper portion of the temporal lobe. This apparently represents the auditory cortex. Since this cortical area in one hemisphere is connected in the symmetrical area on the opposite side, a unilateral lesion is not usually accompanied by disturbance in hearing in either ear. Bilateral lesions on the other hand, lead to complete deafness.

The **acoustic tracts** pass from the cochlea of the inner ear as the cochlear nerve to the medulla and the cochlear nuclei; from these they pass in the striæ acusticæ, corpus trapezoides and lateral lemnisci to the posterior corpora quadrigemina and median geniculate body (Fig. 119) which lies medial to the lateral geniculate body in the subthalamic region. Thence a cerebral path passes to the temporal lobe and to the transverse temporal convolution.

Olfactory impulses pass from the mucous membrane of the nose through the Bulbi olfactorii, and thence, through the fornix in a wide arc, to the cortex in the most anterior portion of the temporal lobe, i.e., the Gyrus hippocampi. Other olfactory tracts pass to the thalamus, which is also connected with the optic tracts and with the sensory cortex in the parietal lobe, and hence may be regarded as a central organ for all sensory impulses.

On the internal aspect of the occipital lobe, about the fissure calcarina, lies the **visual cortex.** This portion of the cortex is distinguished by a white line of medullated nerve fibers. To this visual cortex on each side pass fibers from the homonymous halves of both retinæ, i.e., the right occipital cortex receives fibers from the right half of each retina. Through the posterior portion of the corpus callosum the visual cortex in one occipital lobe is connected with that in the other. The macular area in each retina is apparently represented in the visual cortex in both hemispheres. In case of destruction of one occipital lobe, or a lesion in the region of the calcarine fissure, the visual impulses from the homonymous halves of both retinæ may no longer be perceived and there results **homonymous hemianopsia,** i.e., blindness upon the **same half of each retina** and thereby loss of the **opposite halves of both visal fields.** (Since the rays of light are crossed after entering the eye.) The total destruction of both occipital lobes brings about complete blindness, i.e., cortical blindness.

The nerve fibers bearing visual impulses pass from the retina in the optic nerve and, after partial decussation in the chiasm, as the optic tract to the lateral geniculate body, lying below and somewhat lateral to the pulvinar of the thalamus (Fig. 116). From the lateral geniculate body the cerebral portion of the optic tract passes through the optic

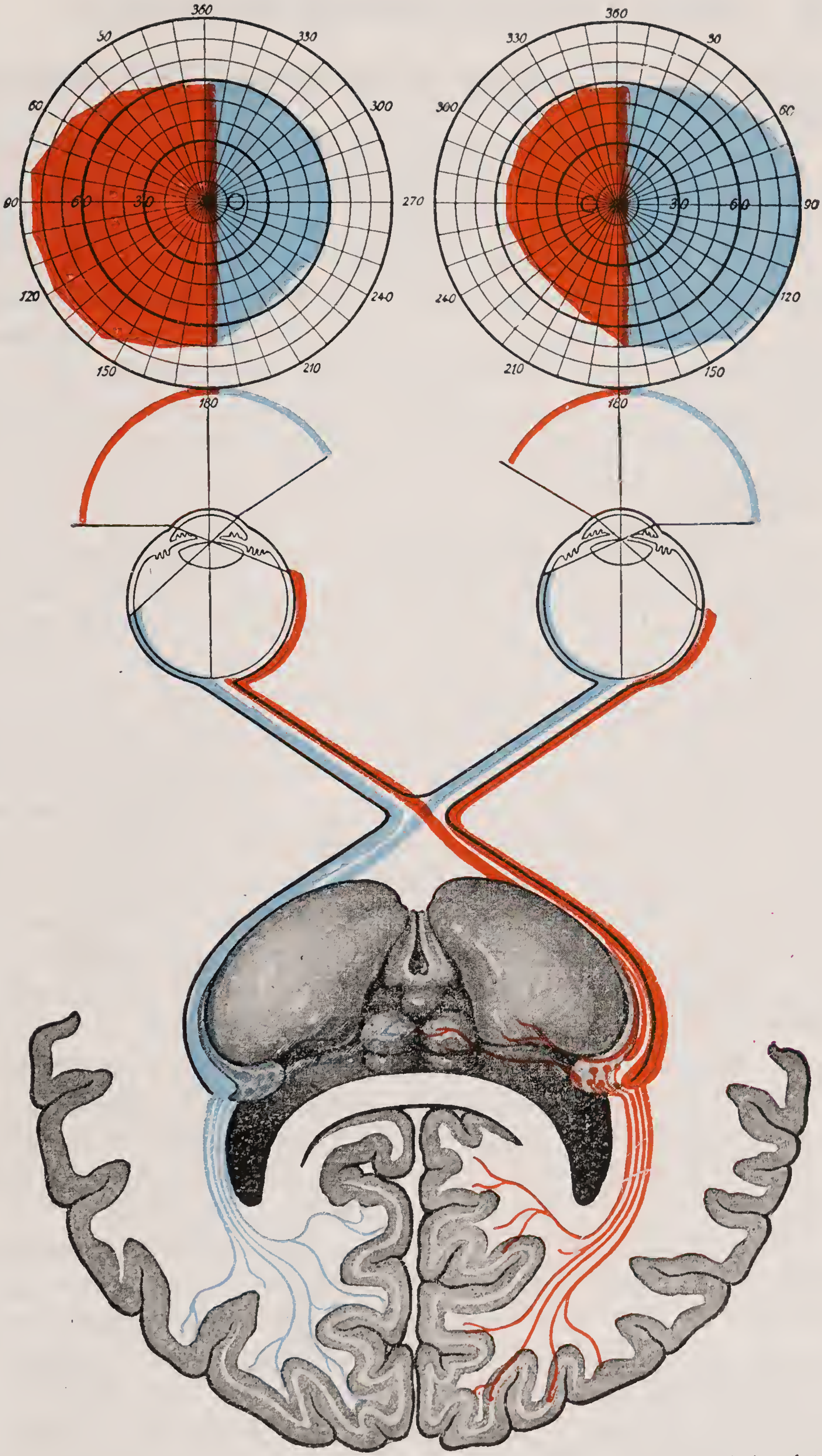


FIG. 116.—Schematic representation of the optic nerves and tracts with their relation to visual fields, corpus geniculatum laterale, thalamus, corpora quadrigemina, and occipital cortex.

radiation to the occipital cortex (cuneus and calcarine fissure).

From the cells of the lateral geniculate body tracts pass to the pulvinar, to the anterior corpora quadrigemina, and to the oculo-motor nuclei beneath the aqueduct of Sylvius. The optic tracts, which transmit the visual impulses to consciousness, course outward from the lateral geniculate body, past the posterior horn of the ventricle to the internal aspect of the tip of the occipital lobe. Interruption of this central optic tract (optic radiation) produces, as does destruction of the visual cortex, hemianopsia involving the opposite half of both visual fields.

Interruption of the crossing fibers in the optic chiasm results in **bitemporal hemianopsia,** i.e., the loss of vision in the **lateral** halves of both visual fields. Since the optic chiasm lies immediately adjacent and anterior to the infundibulum and the hypophysis, tumors in this region are not infrequently accompanied by bitemporal hemianopsia. An acute disease process, e.g., hæmorrhage or softening, interrupting the cerebral optic tract in the depth of the Gyrus angularis, brings about, in addition to hemianopsia, **conjugate deviation,** i.e., deviation of both eyes towards the side of the lesion. Disease of the cortex always occasions deviation of both eyes in the same direction because both are innervated from the cortex in the same fashion. Unilateral paralysis of ocular muscles, and therewith diplopia, never occurs with disease of the cortex alone, but rather with lesions of the nuclei supplying the ocular muscles, or of their nerves. Lesions of the abducens nucleus in the medulla may lead to similar deviation of the eye but always toward the same side, so that when this lesion accompanies hemiplegia the eyes deviate toward the paralyzed side of the body.

Widespread destruction of the cerebral cortex may render coordinated, planned action impossible, e.g., the patient may no longer be able to perform more or less complicated series of movements (eating, dressing, writing, piano playing). Such **motor apraxia** commonly accompanies only lesions of the left frontal region. Motor apraxia involving the left hand may result from interruption of the fibers in the corpus callosum connecting the left hemisphere with the motor area

in the right anterior central convolution. From this fact it is to be assumed that in the organization of complicated acts the left cerebral hemisphere plays the leading part.

With disease of the **frontal lobe** there are observed disturbances of the higher psychic and ethical functions. The frontal lobe also stands in relation to the motor apparatus so that lesions in this area may sometimes produce tremor or ataxia.

The predominant importance of the integrity of the left cerebral cortex is further indicated by the fact that **aphasia** (interference with speech or inability to understand spoken words) results from lesions in this hemisphere. In the event of such a lesion the corresponding areas in the right hemisphere are apparently incapable of adequate function.

Anterior to the lowest portion of the anterior central convolution, i.e., in front of the region supplying the innervation for movements of the tongue, larynx, palate and lips, lies Broca's area. Lesions of this convolution produce **motor aphasia,** i.e., the patient is no longer able to speak intelligibly although the muscles employed in speech are in no wise paralyzed. At the same time the patient is able to understand spoken language clearly, as indicated by the fact that he will correctly follow any given command, though he is unable to repeat words spoken to him. Occasionally, too, the ability to read printed words is lost by patients who were previously able to do so. Only with more wide-spread lesions in this region does the patient lose the ability to understand spoken words or to write from dictation.

Amnesic aphasia is a condition in which, although the patient is able to repeat words spoken by another, he has apparently lost the ability to think of the word which he desires to express. So, for example, a patient may be totally unable to think of the name of a friend or of an object in his environment. If the proper word is spoken to the patient he proceeds to use it correctly. Such a condition sometimes accompanies fatigue or circulatory insufficiency.

In contrast with motor aphasia stands **sensory aphasia,** in which the ability to speak is retained although the ability to understand spoken words is lost. With lesions in the general neighborhood of Heschl's convolution at the posterior

end of the Fossa Silvii and the superior left temporal convolution **word deafness** may occur. Under these circumstances, although hearing is unimpaired, spoken words are not understood. Since such patients cannot always understand their own speech they tend to confuse syllables and words and cannot form intelligible sentences. Such individuals, in contrast to those with motor aphasia, seem to suffer from continual desire to talk, but speak only an unintelligible gibberish (logorrhoea).

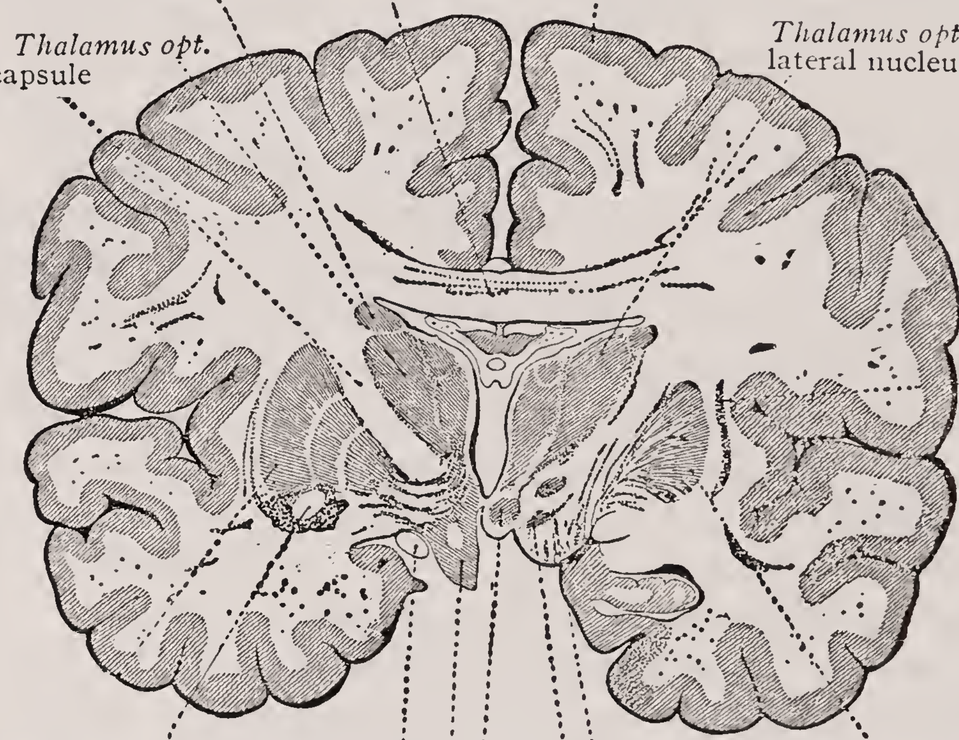


FIG. 117.—Frontal section through the cerebrum.

Circumscribed lesions in the calcarine fissure or the optic tract produce homonymous hemianopsia as described above. A widespread destruction of the left occipital lobe, with interruption of the fibers in the corpus callosum crossing from the right hemisphere, is frequently associated with loss of visual memory, i.e., **optical agnosia** or **mind blindness.** The patient has apparently lost visual memory so that although he sees objects he cannot recognize them. Such agnosia particularly affects the ability to read; **alexia** is thus frequently associated with right-sided hemianopsia. Alexia may also occur if an extensive lesion in the region of the left Gyrus

angularis interrupt not only the optic radiation but also the "association fibers" which connect the occipital and temporal cortex (i.e., the visual and auditory cortex).

All cortical areas appear to be connected by nerve fibers with the basal ganglia, and above all with the thalamus, to which pass, by way of the lemnisci, sensory impulses from all the spinal and cranial sensory nerves. Lesions in the thalamus are therefore associated with disturbances of sensation on the opposite side of the body (and often with spontaneous pain).

In the gray nuclei, which lie beneath the thalamus in the region of the third ventricle, i.e., in the subthalamic centers of the mid-brain and central gray matter, there appears to exist a series of centers, which have to do with the regulation of certain vital functions: the maintenance of normal body temperature, of blood pressure, the regulation of water, sugar and salt metabolism. From these vegetative centers nerve tracts are supposed to pass through the medulla to the spinal cord and thence via the sympathetic and parasympathetic nerves to the skin, muscles and viscera.

The **lenticular nucleus** and the adjacent nucleus caudatus are separated from the thalamus by the internal capsule, but are connected with the thalamus by the ansa lenticularis. These nuclei develop from the floor of the forebrain and, in contrast with the thalamus, have to do with motor function. In the lenticular nucleus several portions are to be distinguished: the putamen and nucleus caudatus which, on account of the gray stria connecting them, are together called the corpus striatum. The corpus striatum becomes medullated at about the same time as the cortex, i.e., during the first half year of life; it is, therefore, to be assumed that neither the corpus striatum nor the cerebral cortex assume their normal function until sometime after birth. The globus pallidus contains many medullated nerve fibers at birth and is assumed to be functioning at that time. From the globus pallidus pass nerve tracts to certain subthalamic centers, to the corpus luysii, the substantia nigra, the red nucleus and the spinal cord. Since the new born child is already capable of certain more or less complicated motor functions, such

as crying, sucking and swallowing it is to be assumed that the globus pallidus represents a primitive motor center.

As the medullation of the corpus striatum proceeds, during the first year of life, the motor functions of the child become coordinated. Posture is thus maintained, first as the child sits, later as he creeps, stands or walks. Even after the

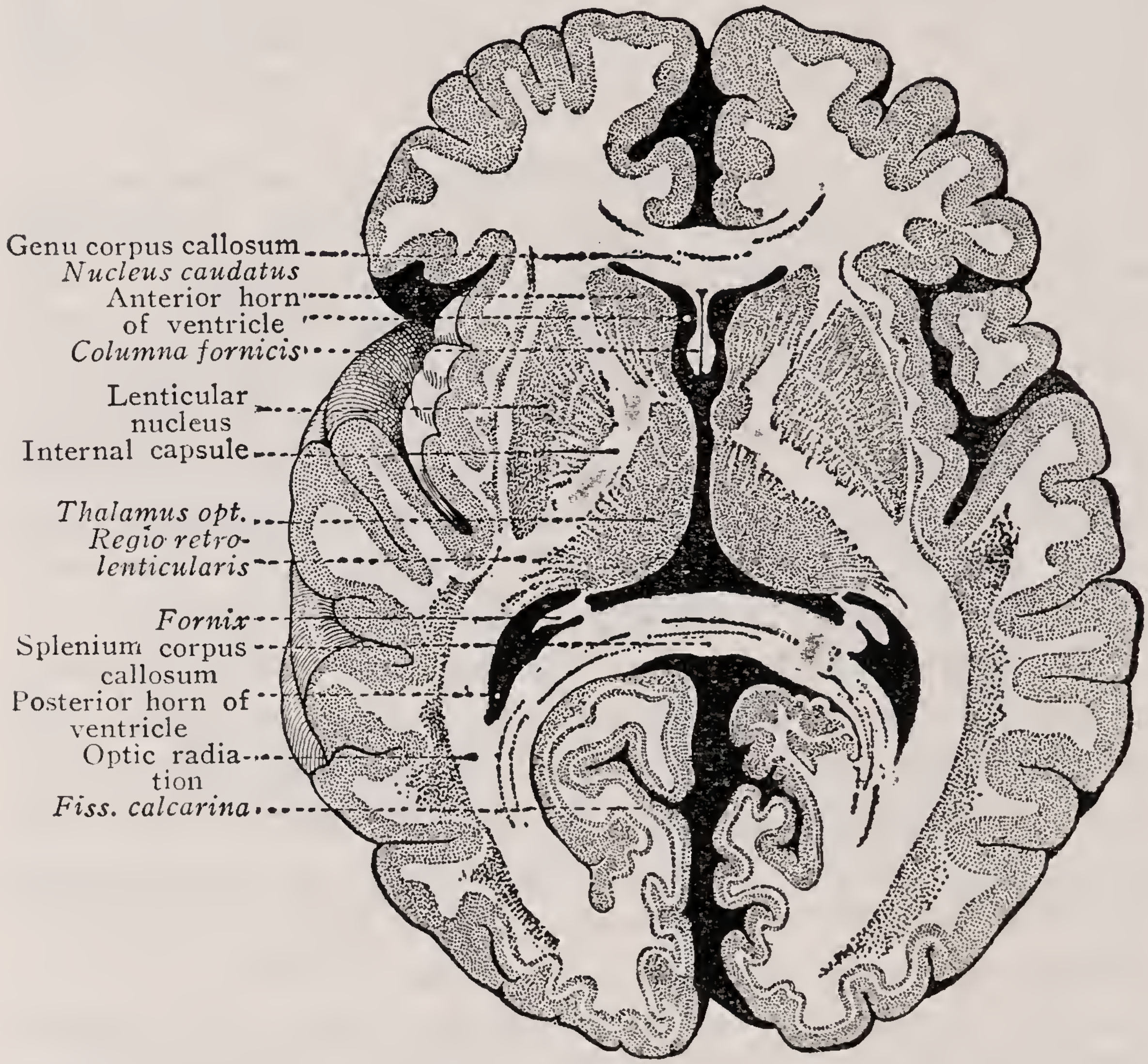


FIG. 118.—Horizontal section through the cerebrum.

cortical centers have developed and voluntary purposeful movement has become possible, the corpus striatum and globus pallidus continue to control certain automatic motor functions below the level of consciousness. Such include coordination of movements of the trunk and extremities in walking, lifting, etc. In addition involuntary movements and tone of the facial muscles, which define facial expression, appear to be controlled by these centers.

The motor centers in the basal ganglia, together with the

corpus Luysii, red nucleus, substantia nigra, and their connections with the cord constitute the **extrapyramidal motor system.**

With disease of the lenticular nucleus and the other "extrapyramidal motor nuclei," i.e., the subthalamic body (Luys), the substantia nigra and the red nucleus, all automatic motor functions are disturbed or impaired; in contrast with this, lesions of the pyramidal system involve those functions which are normally under voluntary control. Complete destruction of the lenticular nuclei, e.g., as a result of softening or sclerosis, causes a peculiar **stiffness** (rigor) of the musculature with limitation of movement of the trunk and extremities, and also slow dysphonia and dysphagia. Affecting the muscles of the face this causes a peculiarly immobile "mask-like" expression. **"Wilson's disease"** is characterized by gradual progressive degeneration of the lenticular nucleus associated with cirrhosis of the liver. In some forms of disease of the lenticular nucleus, particularly those involving the globus pallidus, involuntary **choreic movements** are sometimes observed, and, with degeneration of the putamen, **athetoid movements.** The same holds true of lesions of the superior cerebellar peduncles which connect the cerebellum to the red nucleus and the thalamus.

In chorea minor (Sydenham), or St. Vitus' dance, which is associated with rheumatic fever in children, as well as in chorea gravidarum in young primiparae, and occasionally with apoplexy in elderly people, lesions in the region of the lenticular nucleus are associated with the involuntary choreic movements. In Huntington's chorea (hereditary) chronic degeneration of the putamen has been described.

The **cerebellum** is connected with the cerebrum by two main paths: (1) Through the large middle peduncles which arise in the frontal and temporal lobes and pass through the internal capsule to the nuclei in the pons and in the lateral lobes of the cerebellum. This connection of the cerebellum with the frontal lobe probably plays an important part in the coördination of voluntary movement. (2) The **dentate nucleus** in the middle cerebellar lobe is connected by the superior cerebellar peduncle with the red nucleus and the optic thalamus; on the opposite side, this tract carries pre-

FIG. 119.—Midbrain with anterior corpora quadrigemina, red nucleus, substantia nigra and cerebral peduncles in relation to corpus geniculatum mediale and laterale, and N. opticus; section also shows relation of the subarachnoid space to the Pia and to the cerebral ventricles.

sumably regulating impulses to these centers. A third cerebellar peduncle passes from the medulla as the restiform body, and carries sensory tracts from the cord to the cerebellum. By means of this apparatus the cerebellum plays a part in general coördination. It regulates the finer mechanisms of movements, their proper timing and adjustment. In particular the middle (embryologically older) portion of the cerebellum controls synergy of all muscular movements and the muscle tonus which automatically govern the maintenance of equilibrium in walking, sitting or standing. This apparatus, with that of the labyrinth, makes possible orientation in space and the maintenance of equilibrium.

Disease of the cerebellum is manifested by **asynergy** and **hypotonus** of those muscles whose proper innervation is essential to coördinate movement, e.g., the coördinate movement of a leg or of the trunk in walking, and results in **cerebellar ataxia.** This cerebellar ataxia is apparent not only upon walking or standing but also while sitting. The gait is **stumbling** and **staggering** like that of a drunken man. **Dizziness** and **vertigo** are also characteristic. Babinski has described a symptom of cerebellar disease which is called **adiadochokinesis**; this consists in inability to carry out rapid and repeated antagonistic movements, e.g., supination and pronation, or flexion and extension of the hand. However, this symptom also appears in various spastic paralyses and in other disturbances of coördination and innervation, e.g., multiple sclerosis, disease of the lenticular nucleus with athetosis.

Upon the dorsal surface of the **midbrain** lie the corpora quadrigemina. Beneath the Aqueduct of Sylvius, which connects the third and fourth ventricles, are the motor nuclei from which are innervated the extraocular muscles. The massive **cerebral peduncles** contain the pyramidal tracts and, in their median and lateral portions, tracts which pass from the cerebrum to the pons and thence to the cerebellum. Above these lie the sensory tracts, which compose the **median leminisci,** and above these the red nuclei and cerebellar peduncles. Lesions in the midbrain lead to oculomotor palsy with diplopia, ptosis and interference with the pupillary reflex. Extensive lesions involving the cerebral peduncles

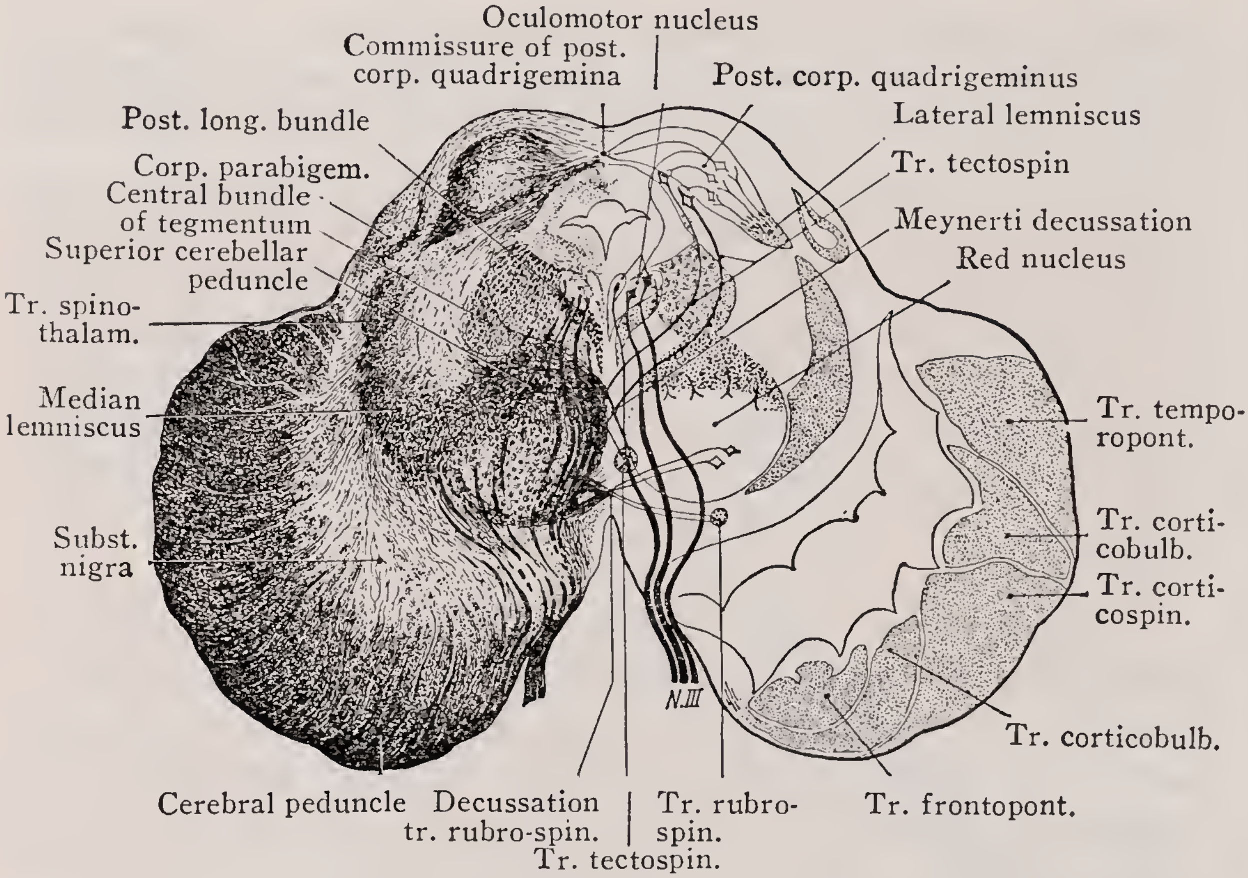


FIG. 120.—Region of posterior corpora quadrigemina.

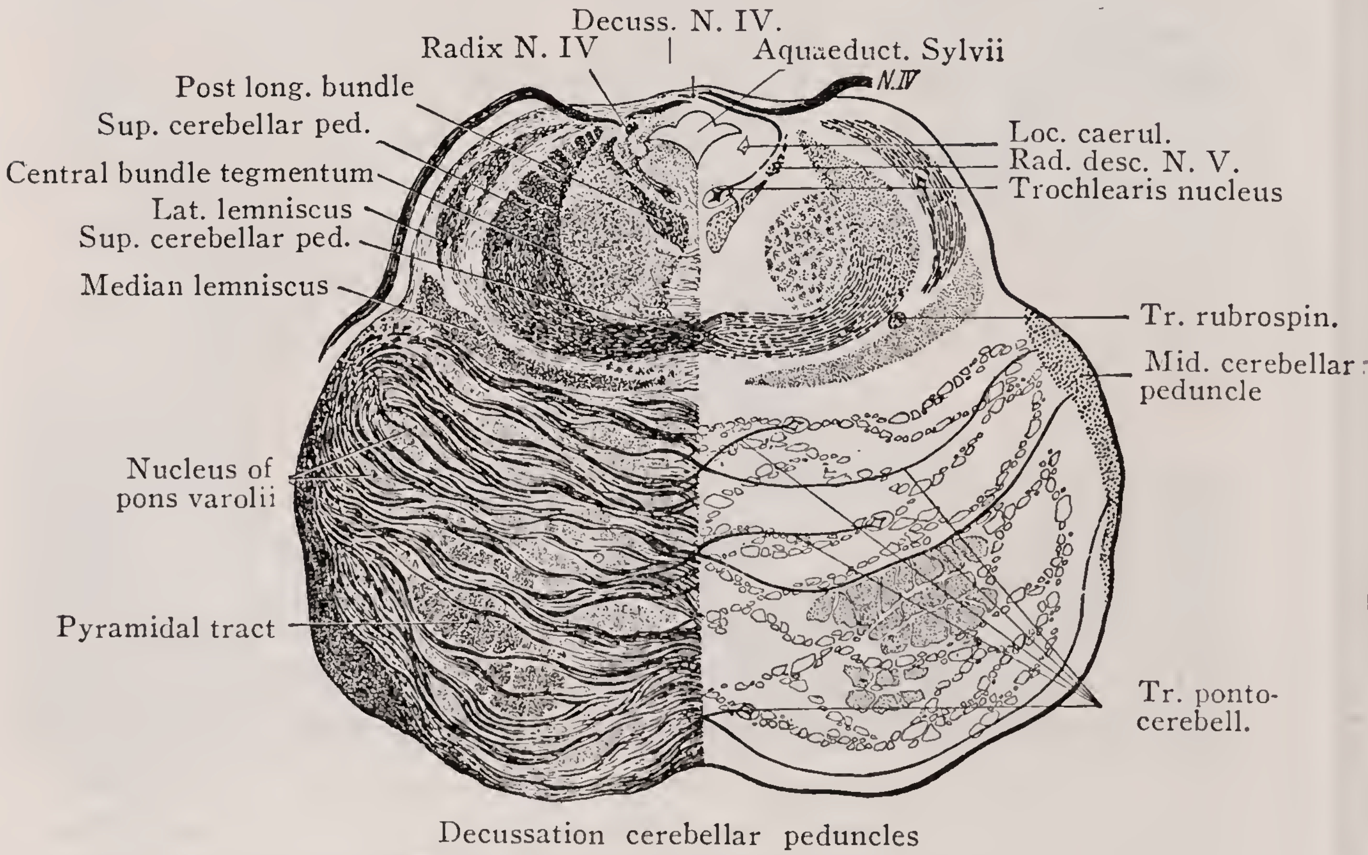


FIG. 121.—Region of pons with nucleus N. IV.

are associated with oculomotor palsy on the side of the lesion and hemiplegia and hemianesthesia on the opposite side.

In the region of the pons, beneath the cerebellum, the acqueduct of Sylvius broadens out into the fourth ventricle, under the floor of which lies the abducens nucleus, which innervates the lateral rotation of the eye. The coördination of ocular movements is accomplished by the posterior longitudinal bundle connecting the nuclei of the oculomotor, trochlear, and abducens nerves. From the middle of the pons arises the large root of the fifth nerve, the motor and sensory nuclei of which lie dorsal to the pons. The sensory nucleus of the fifth nerve extends downward, well into the medulla. Sensory disturbances over the face may therefore be caused not only by lesions in the region of the pons but also by lesions in the medulla. At the lower end of the pons, and in the upper portion of the medulla, lies the nucleus of N. facialis. In the angle between the pons and the medulla lie also the nuclei for the Nn. acusticus and vestibularis. The latter receives fibers from the semicircular canals, and from it pass tracts to the cerebellum, by way of Deiter's nucleus in the angle between the medulla and the cerebellum.

Beneath the floor of the fourth ventricle also lies the nucleus hypoglossus, whence motor fibers pass to the ventral surface of the medulla emerging next to the pyramidal tracts, and thence to the muscles of the tongue. Lateral to the nucleus hypoglossus lies the vagus nucleus, whence autonomic fibers pass to the abdominal and thoracic viscera. The sensory nucleus of the vagus lies next to the nucleus glossopharyngeus and receives fibers from the pharynx, larynx, trachea and oesophagus. The motor nucleus of the vagus (nucleus ambiguus) supplies motor fibers to the pharynx, larynx and oesophagus. The various vagus nuclei stand in close functional relationship to the substantia reticularis of the medulla, in which are supposed to be located centers for regulation of respiration, circulation and blood pressure.

The motor pyramidal tracts lie as bundles beneath the ventral surface of the medulla. At its lower end they undergo almost complete decussation, passing to the lateral columns

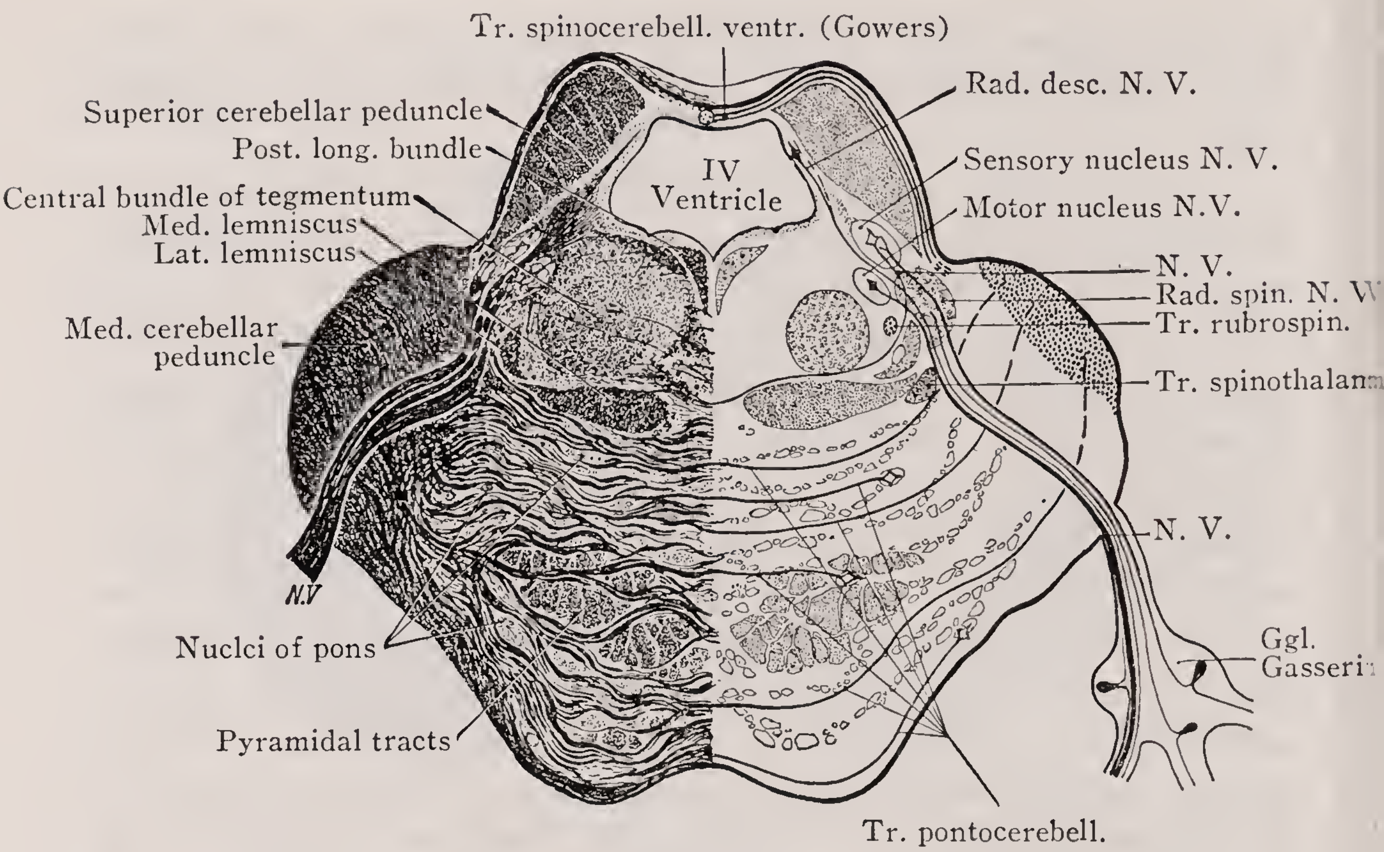


FIG. 122.—Region of pons with cerebellar peduncles, fourth ventricle and roots of N. V.

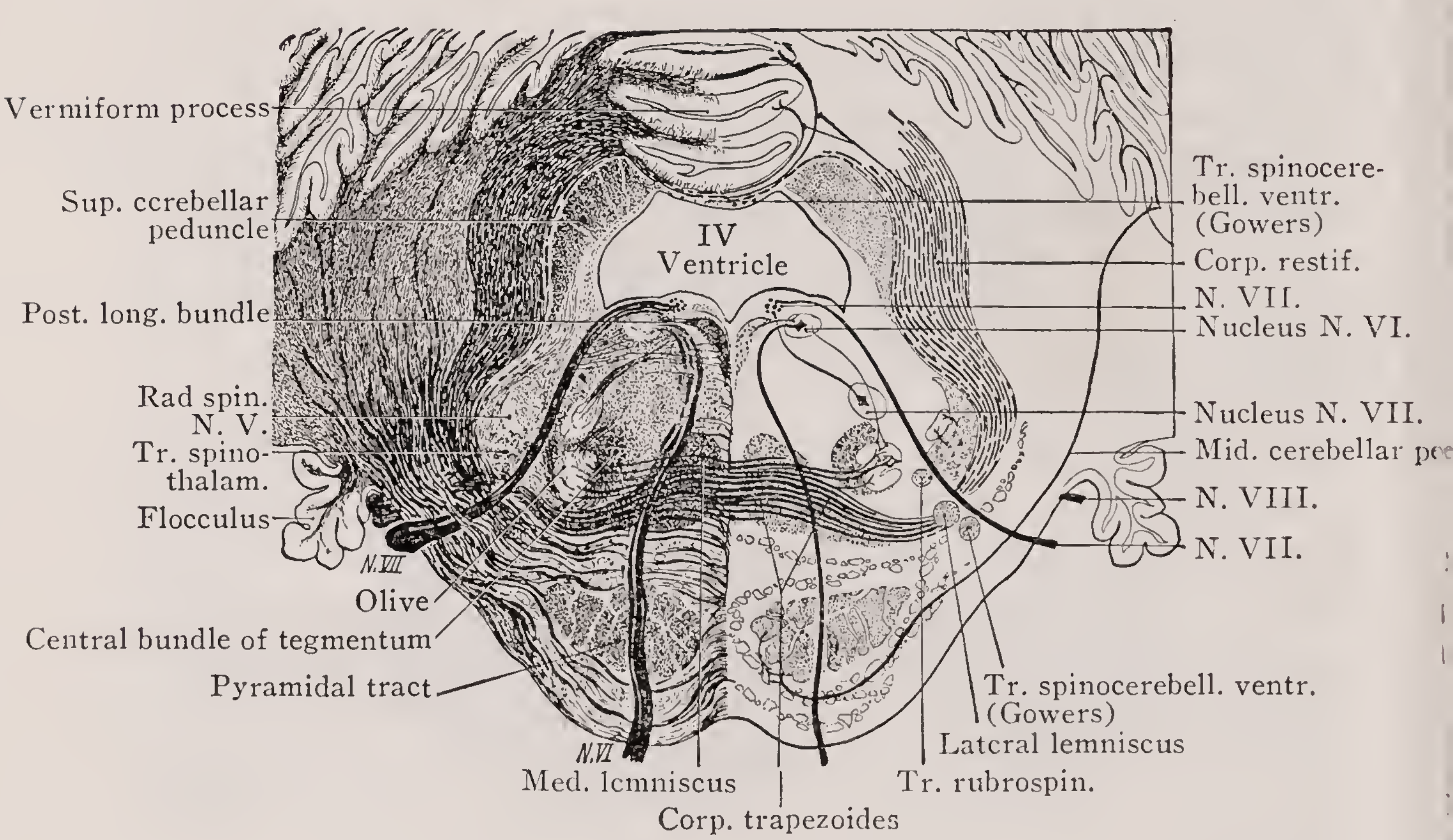


FIG. 123.—Region of lower end of pons with nuclei Nn. VI and VII.

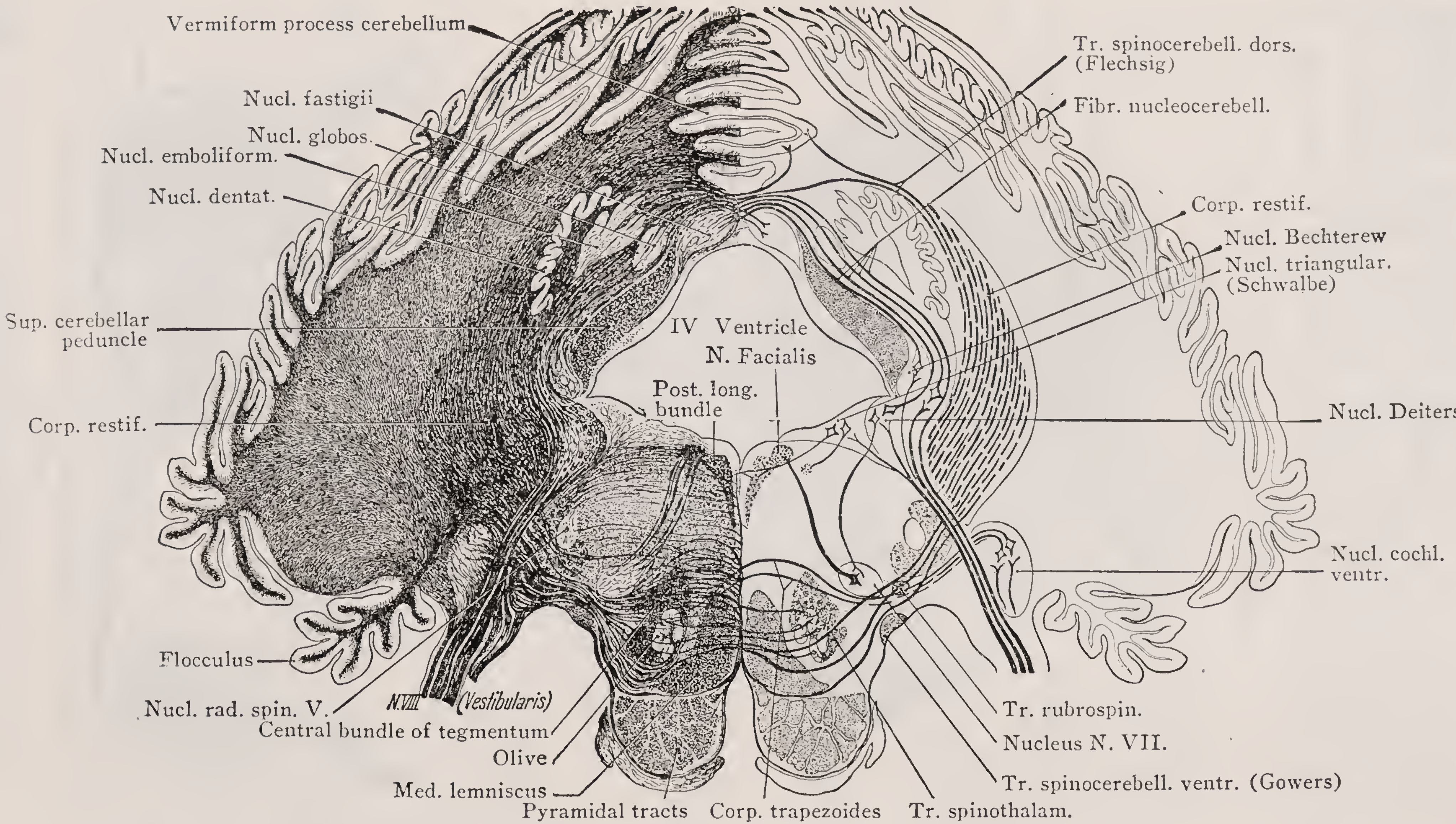


FIG. 124.—Region of upper end of medulla showing relation to cerebellum.

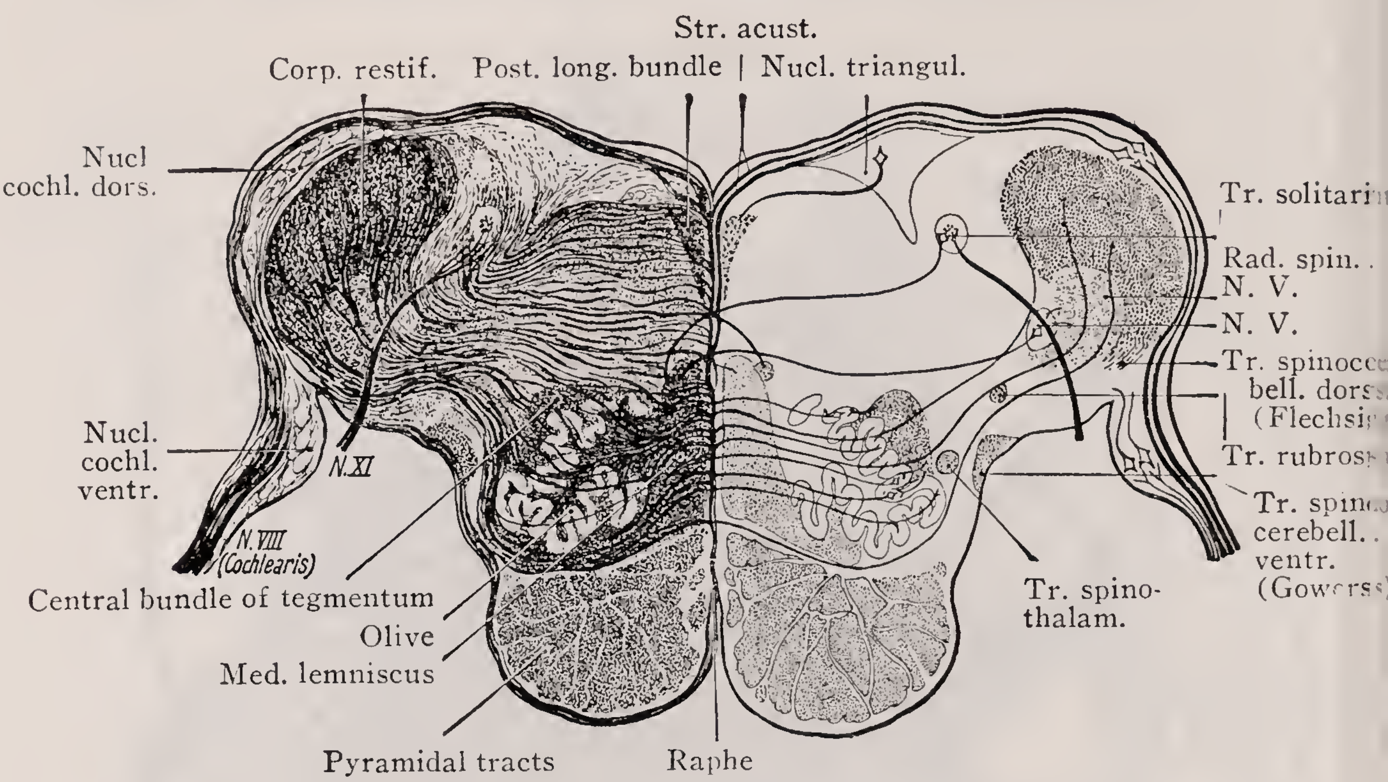


FIG. 125.—Medulla with N. VIII and its nuclei, and N. XI.

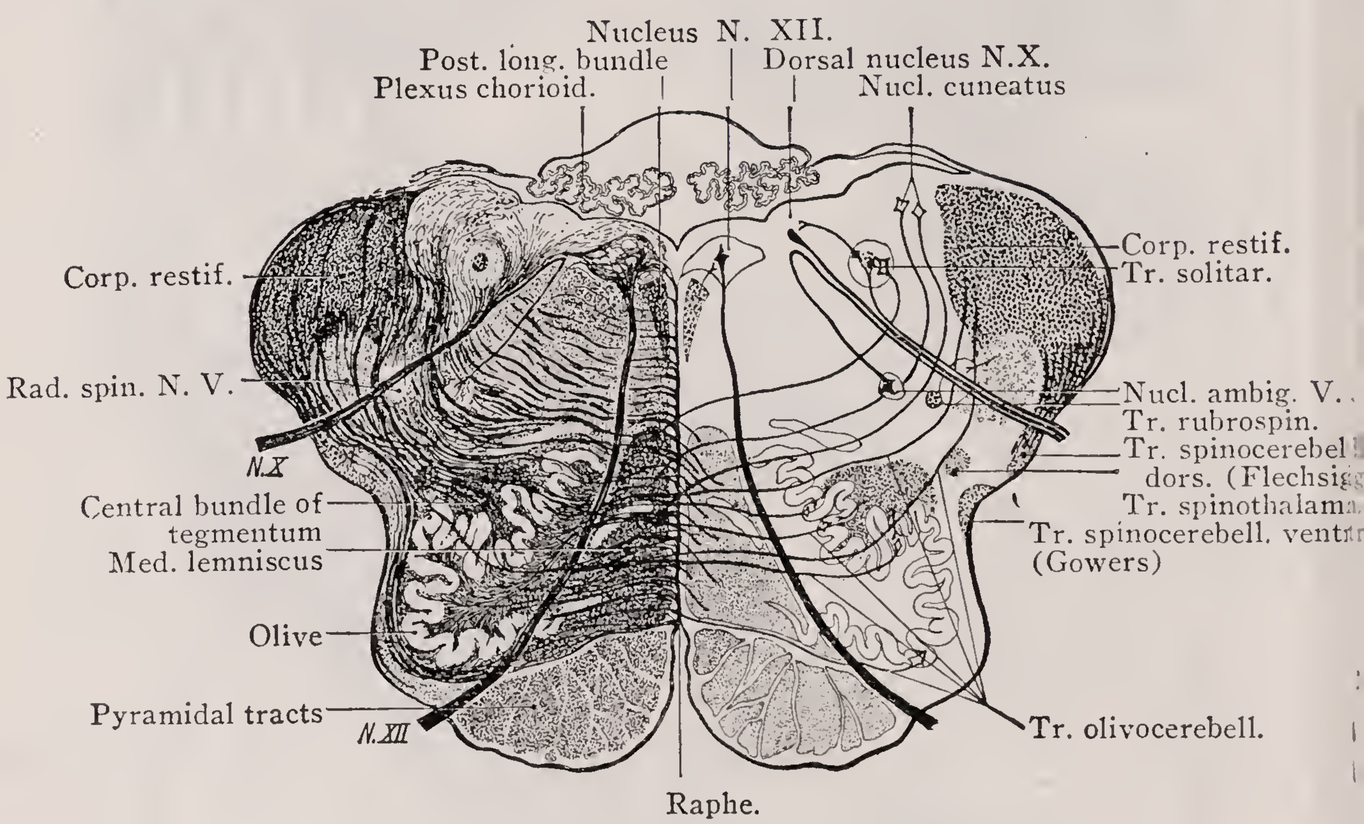


FIG. 126.—Medulla with nuclei of Nn. X and XII.

of the cord on the opposite side. Only a small portion of the pyramidal tract passes down to the cord on the same side. Decussation of the sensory paths from the posterior columns of the cord takes place just above the pyramidal decussation via the arcuate fibers.

The **spinal cord** does not occupy the spinal canal for its entire length; the lower end of the cord, the conus terminalis, lies at the level of the first lumbar vertebra. The first lumbar segment lies opposite the spinous process of the 10th or 11th thoracic vertebra, the first dorsal segment opposite that of the 6th or 7th cervical vertebra. The anterior and posterior roots course downward from their point of exit from the cord to the appropriate foramen, in which lies the intervertebral ganglion of the sensory root, and through which

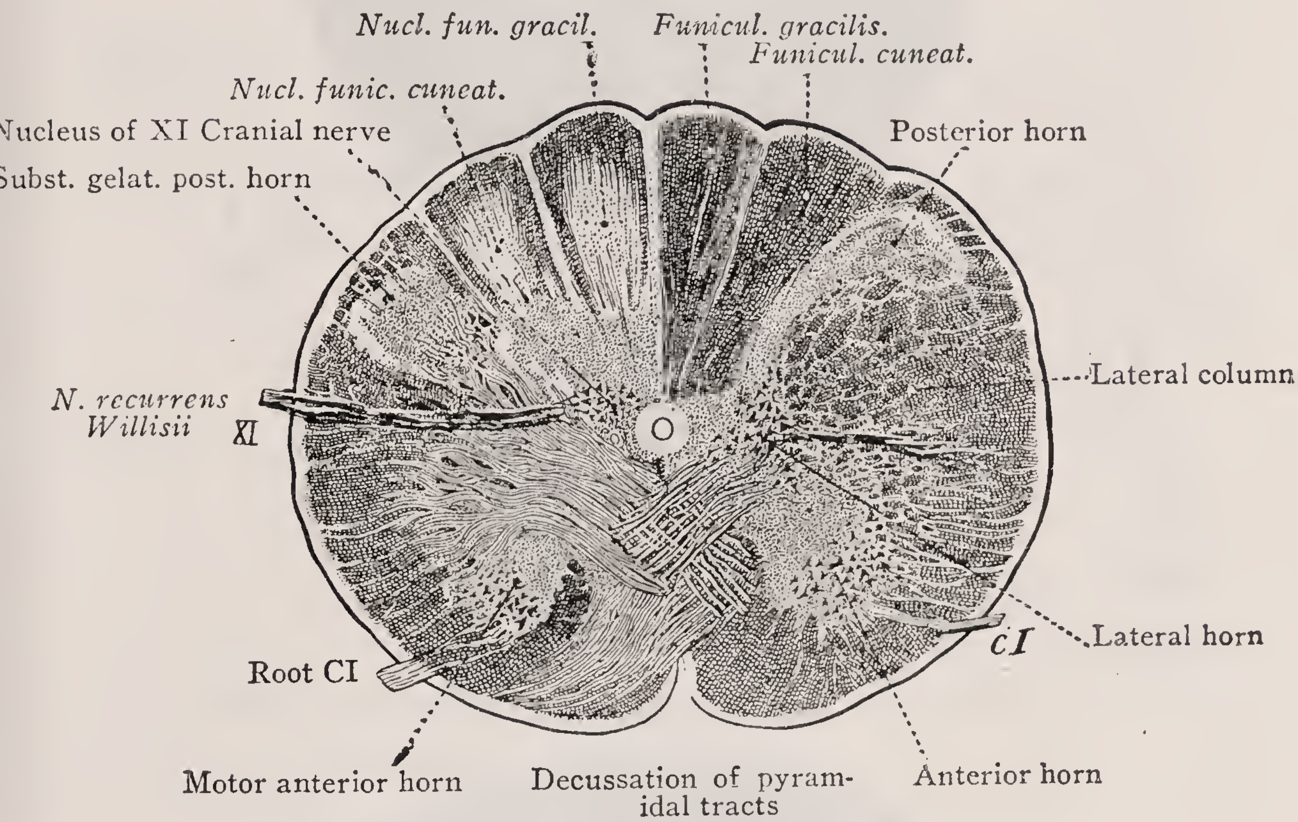


FIG. 127.—Medulla at decussation of pyramidal tracts.

the nerve passes to the periphery. The roots of the lower lumbar and sacral segments form the cauda equina; the sacral roots pass downward to emerge through the sacral foramina (see figure 133).

The gray matter of the spinal cord encloses the central canal. In contrast with the ventricles of the brain the spinal canal does not serve for the circulation of the cerebro-spinal fluid. This collects in the spinal subarachnoid space which extends well down within the sacral vertebrae.

In the gray substance of the anterior horn of the spinal cord lie groups of large motor ganglion cells, whose axis cylinders leave the cord in the anterior roots and pass to the muscles. In the angle between anterior and posterior

horns are clumps of small ganglion cells from which axis cylinders pass also in the anterior roots as white rami communicants to the sympathetic ganglia of the paravertebral chain, providing innervation to blood vessels, glands, etc.

FIG. 128.—Cervical cord.

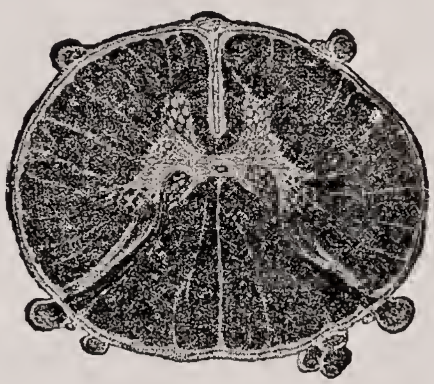


FIG. 129.—Thoracic cord.

FIG. 130.—Lumbar cord.

The posterior horns of the gray substance have to do with sensory function. From them numerous connecting paths pass to the anterior horn; these are presumed to be associated with reflex function. In addition tracts arising from the ganglion cells in the posterior horn cross the mid-

line and pass upward in the anterior columns on the opposite side of the cord. The posterior columns are almost exclusively concerned with conduction of deep sensibility.

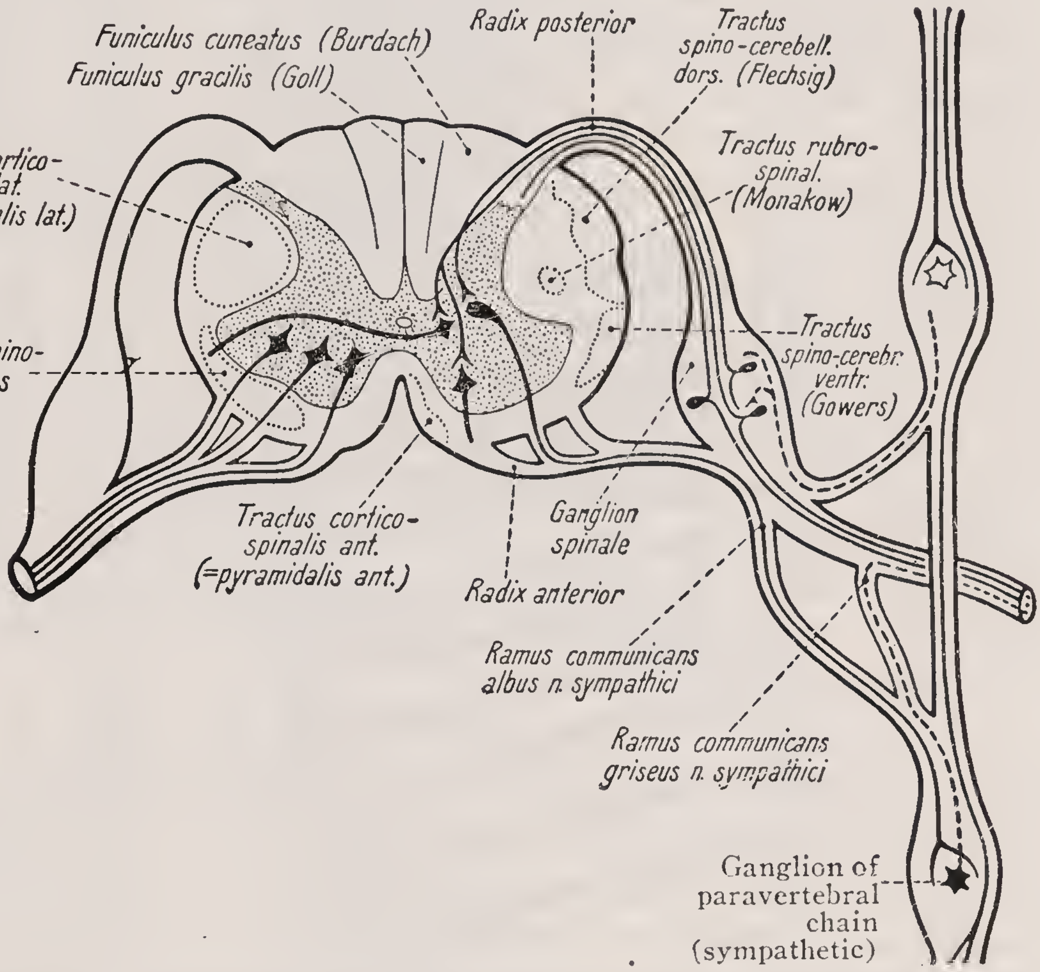


FIG. 131.—Diagram of spinal cord and connections with sympathetic nervous system.

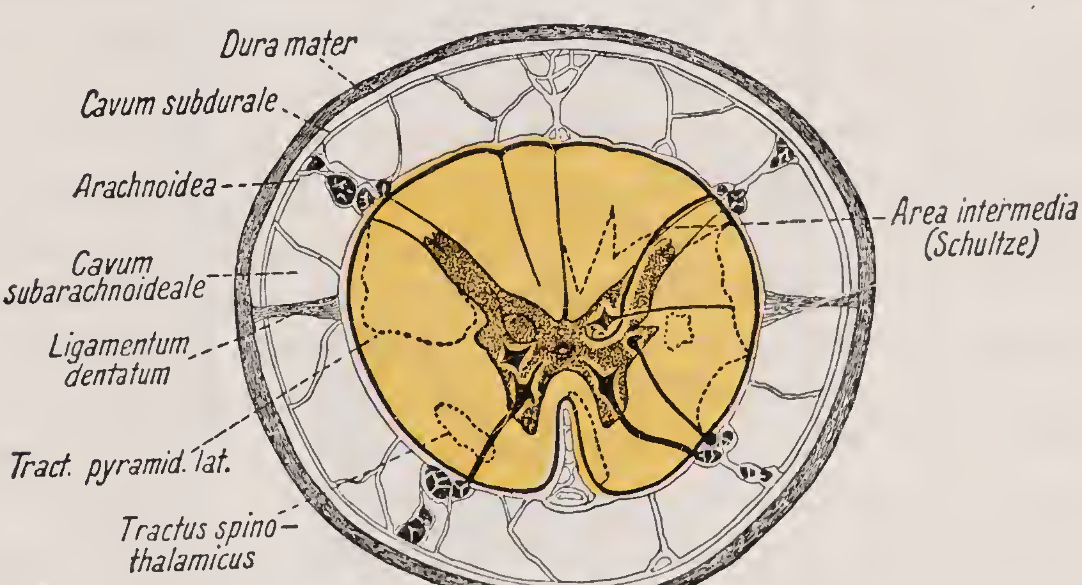


FIG. 132—Medulla spinalis, pars dorsalis.

The trophic center for a peripheral **sensory nerve** lies in the intervertebral ganglion. From this point inward the sensory paths pass through the posterior roots into the cord

and, in part, directly to the posterior column on the same side in which they course upward uncrossed to the medulla. Since the newly entering fibers from each segment tend to lie immediately adjacent and medial to the posterior horn in the posterior columns those from the lower (sacral and lumbar) segments are displaced toward the mid-line in the thoracic and cervical cord (Columns of Goll) while those from upper segments lie lateral to these (Columns of Burdach). A second portion of the posterior root passes into the gray substance of the posterior horn and, within 5–6 segments above its point of entry, crosses through the gray substance near the mid-line to pass upward in the antero-lateral column of the opposite side. It is to be assumed that deep sensibility is conducted through the posterior column of the same side, touch in part in the posterior column of the same side but chiefly in the opposite antero-lateral column, and pain and temperature exclusively in the antero-lateral column after crossing.

The columns of Goll and Burdach terminate in nuclei in the medulla, from which fibers pass across the mid-line to join with the sensory tracts from the cord which have already crossed. From this point upward the sensory tracts course as the **median lemniscus** through the medulla, pons and peduncles to the ventral and lateral nuclei of the thalamus. Thence other fibers pass upward through the internal capsule and corona radiata to the cortex of the posterior central convolution and the remainder of the parietal lobe. In the postero-lateral columns of the cord lie the pyramidal tracts, i.e., long axis cylinders arising from cells in the anterior central convolution which course via the internal capsule and cerebral peduncles to end about cells in the anterior horn of the cord; these motor fibers control voluntary movement. Upon section the pyramidal tracts degenerate downward even to the lowermost sacral segment. Anterior to the pyramidal tracts in the lateral columns are other efferent tracts which presumably govern certain motor functions below the level of consciousness.

With **complete section** of the cord the **posterior columns degenerate upward** from the point of the lesion, particularly

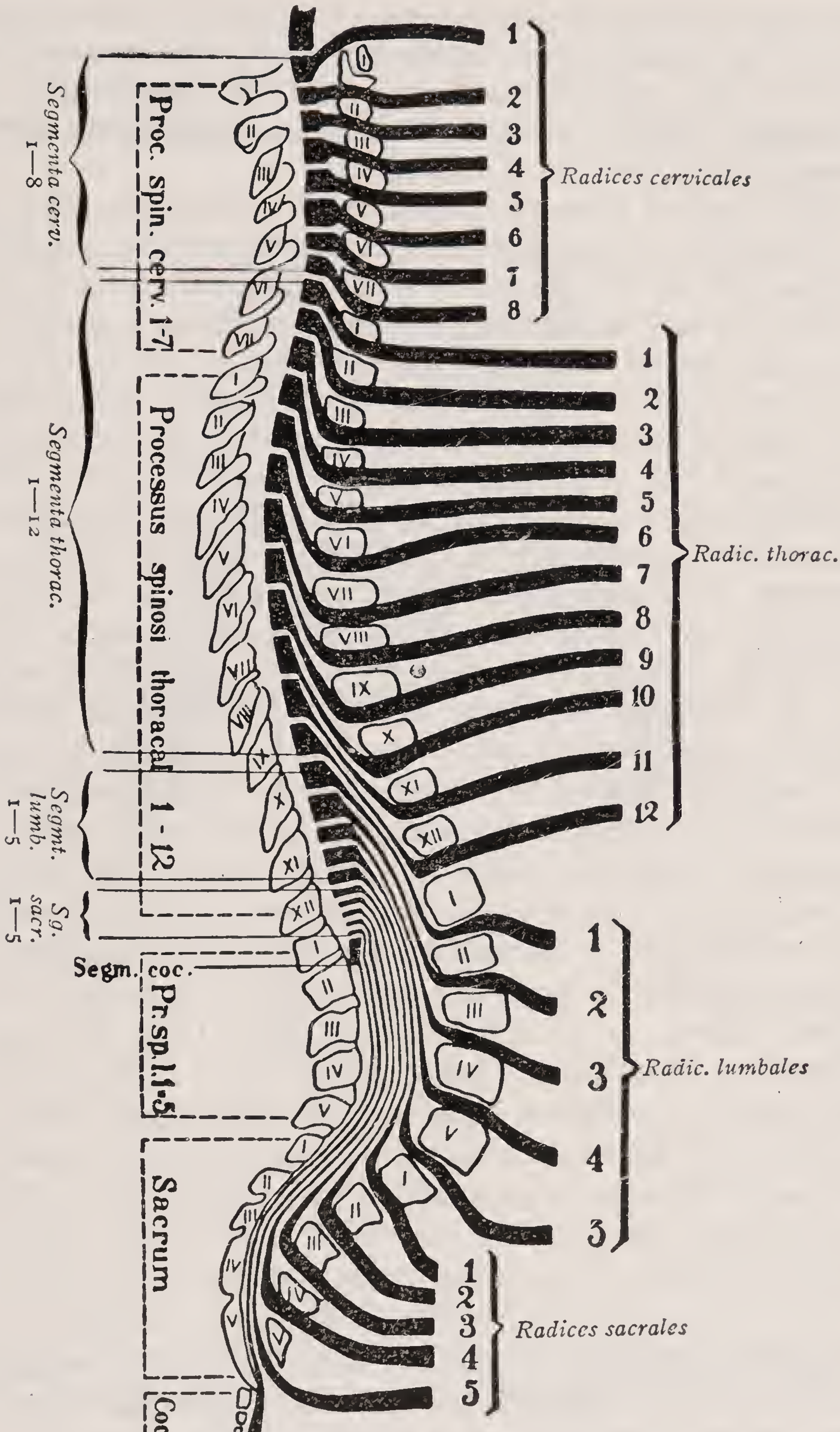


FIG. 133.—Topographical relations of spinal cord segments to vertebral bodies, spinous processes and points of exit of spinal roots (after Bing: Kompendium der topischen Gehirn und Rückenmarksdiagnostik). Reproduced by permission of the publisher.

the tract of Goll and the cerebellar tract in the lateral column as well as Gower's tract, which represents also an ascending path to the corpora restiformia and the cerebellum; the **pyramidal tracts,** lateral and anterior, **degenerate downward** from the level of the lesion.

Each pair of anterior roots emerging from the cord and the posterior roots at the same level correspond to a definite segment of the cord; one may regard the cord as made up of a series of such segments or metameres. From a study of a large number of cases of transverse section of the cord it has been possible to determine which muscles are supplied from each of these segments (and from which anterior roots), and also to link up certain skin areas with the sensory fibers of certain definite posterior roots. Since the peripheral nerves interweave considerably in the brachial, lumbar, and sacral plexuses, the muscle groups which receive their motor supply from any given segment of the cord are arranged quite differently from those supplied by a given peripheral nerve, e.g., N. radialis or medianis. The same is true of the sensory areas in the skin; the area supplied from a single spinal cord segment does not correspond accurately to the distribution of any single cutaneous nerve; the cutaneous areas are arranged horizontally about the trunk like a girdle forming an acute angle with the intercostal spaces. In the extremities the arrangement of the sensory segments is best understood if one considers the arms and legs held perpendicular to the spinal column, as in four-footed animals. Over the upper extremities these sensory zones are arranged in the form of long bands covering the outer portion of the upper arm, the radial side of the forearm and the thenar side of the hand in the case of the upper segments (C6–C8), and the ulnar side of the hand and forearm, the inner side of the upper arm and axilla in the case of the segments immediately below (Th. 1–Th. 3). In the lower extremities the anterior surface of the thigh and lower leg are supplied from the lumbar segments and the posterior surface of the same from the sacral segments. The perineum, which in four-footed animals represents the most posterior portion of the body receives its sensory supply from the lowest portion of the cord (N. pudendus internus).

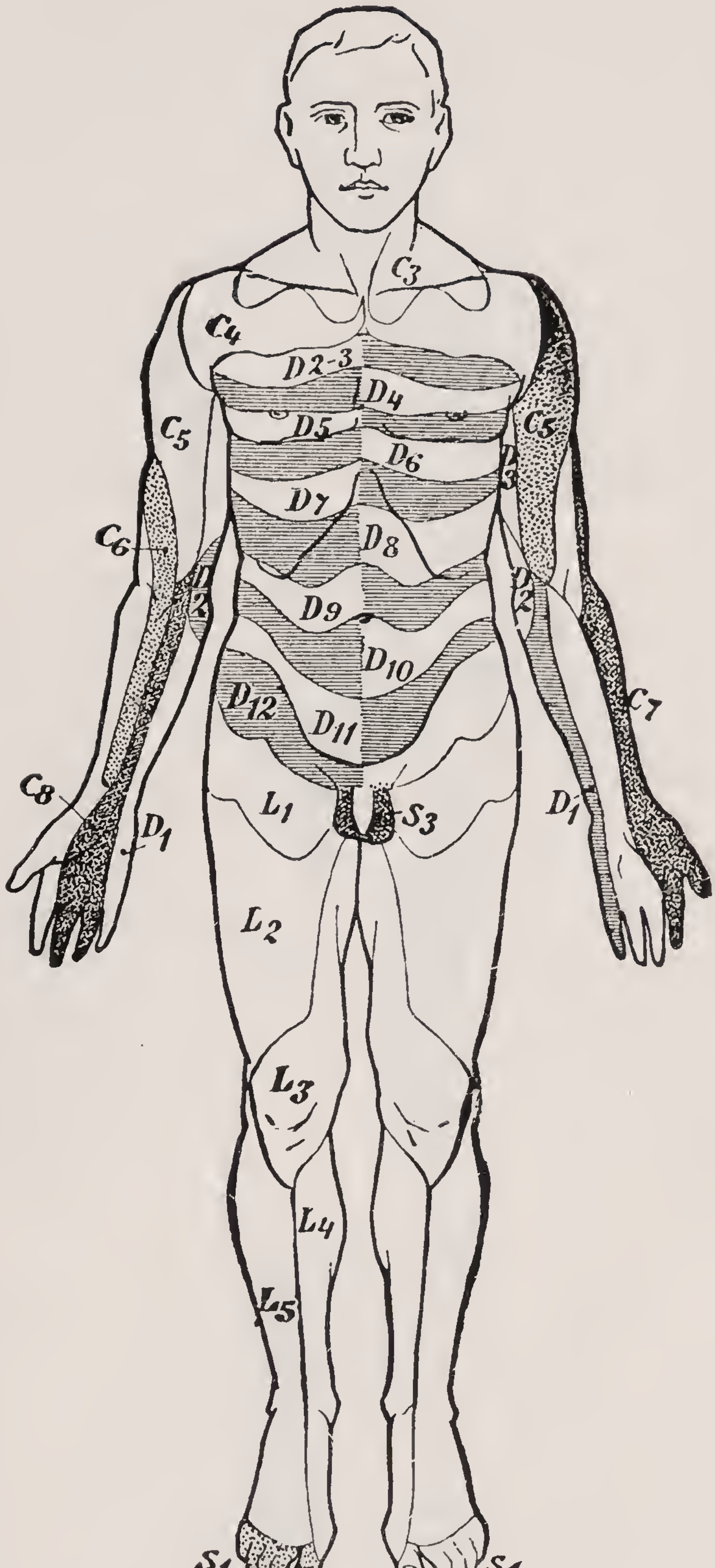


FIG. 134.—Cutaneous sensory areas corresponding to the various segments of the cord. The letters C, D, L and S indicate zones deriving sensory innervation from cervical, thoracic, lumbar and sacral segments respectively. (Shaded and dotted areas for contrast only.) *Figure is drawn after Head.*

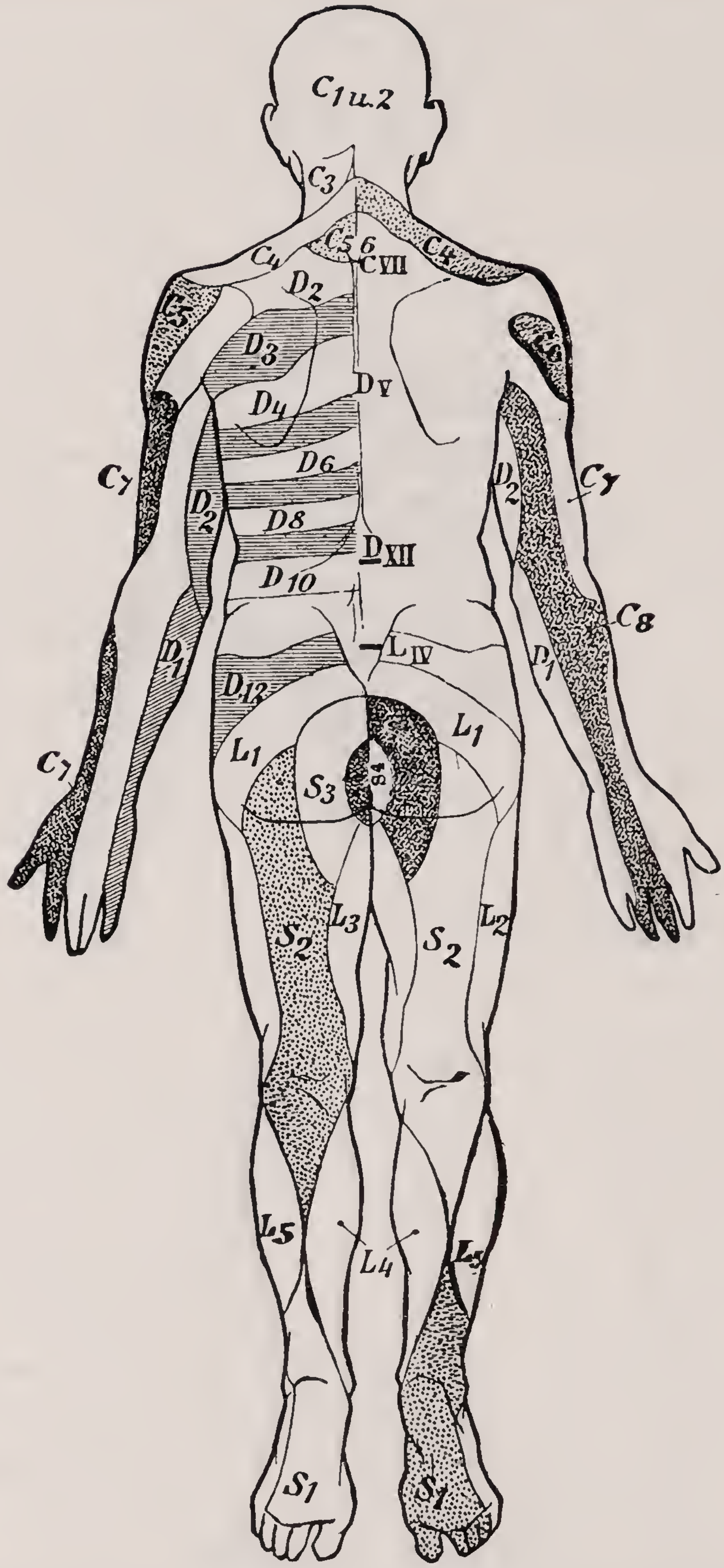


FIG. 135.—Arabic numerals indicate cord segments (e.g., C4 =distribution from the 4th cervical segment). Roman numerals on right, CVII, DV and XII, and LIV indicate spinous processes of 7th cervical, 5th and 12th thoracic and 4th lumbar vertebræ respectively. These serve as points of orientation.

In order accurately to localize, in the case of disease of the cord, the level of the pathological process it is necessary to understand the arrangement of the motor, sensory and reflex functions in the various cord segments. Figures 134 and 135 together with the tables on pages 418–21 summarize this information. It is to be noted that the cutaneous area supplied by a single cord segment is somewhat overlapped by both its neighbors so that, with destruction of a single pair of posterior roots, the corresponding skin area is not completely anæsthetic. The same is true of motility, since the source of innervation of a muscle and particularly of a long muscle is not confined to a single cord segment but is represented in the segments immediately above and below, or, in the case of a very long muscle, in a whole series of segments. For this reason various observers and text books disagree in many details.

It is apparent that with complete transection of the cord, e.g., with transverse myelitis or tumor, there is lost not only the function of the injured area but also the voluntary movement and sensibility of all portions below it. So, for example, with destruction of the mid portion of the cervical cord: Paralysis of upper and lower extremities, sensory disturbances below the shoulders, accentuation of the knee-jerks, ankle clonus, positive Babinski, urinary and fæcal incontinence. With disease of the 5th thoracic segment paralysis of the legs, anæsthesia below the 8th thoracic vertebra and nipples, accentuation of the knee jerks, ankle clonus, positive Babinski, urinary and fæcal incontinence. With a lesion in the midlumbar cord the legs are paralyzed, patellar reflexes lost, ankle clonus and positive Babinski present, anæsthesia of the lower legs, the posterior portion of the lower leg and thigh and of the perineum, urinary and fæcal incontinence. Destruction of the **sacral cord** produces the so-called **saddle anæsthesia:** Destruction of the 3rd and 4th sacral segments (conus terminalis): No paralysis of the legs, anæsthesia of the perineum, urinary and fæcal incontinence, loss of the anal reflex. Destruction of the conus terminalis is most frequently produced by trauma, e.g., from a fall landing in the sitting position.

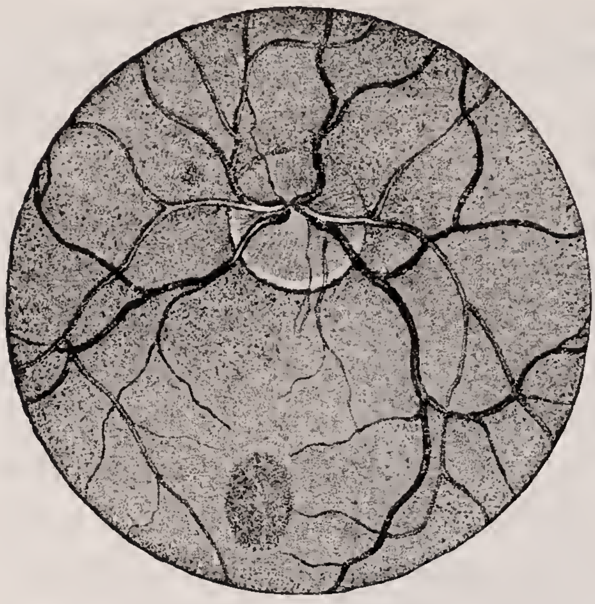


Fig. 136.—Normal fundus oculi.

Fig. 137.—Atrophy of N. opticus with tabes dorsalis.

Fig. 138.—Neuritis optica.

Fig. 139.—"Choked disc."

Fig. 140.—"Albuminuric retinitis.'

Cranial Nerves

Olfactorius. The sense of smell is tested by exposure to various odoriferous, but not irritating, substances (ether, asafœdita, perfume, etc.).

Opticus. Concerning the anatomical course of the optic tracts see page 384. Visual acuity is tested, when necessary, after correction of myopia and hypermetropia; visual fields (see page 384) and color vision are then examined, and finally ophthalmoscopic examination is made.

With atrophy of the optic nerve the papillæ appear porcelain white. With tabetic (syphilitic) optic atrophy the nerve head is sharply outlined and the vessels unaltered; with atrophy following optic neuritis and papillœdema due to increased intracranial pressure the outlines of the papillæ are obscured, the arteries narrowed, the veins dilated and tortuous. With early optic atrophy the perception of color, particularly of red and green, is disturbed and the visual fields are irregularly reduced in size; with severe optic atrophy vision is impaired, sometimes to the extent of complete blindness. Choked-disc, a bulb-like protrusion of the swollen nerve head into the optic bulb, with narrowing of the arteries, tortuosity and dilatation of the veins, occurs with intracranial tumors or with any long-standing increase in intracranial pressure. Optic neuritis is found with nephritis, leukæmia, polyneuritis, and lead poisoning.

Oculo-motor supplies Mm. levator palpebral superioris, rectus superior, medialis and inferior, obliquus inferior and sphincter pupillæ; also, through the ciliary ganglion, the ciliary muscle which controls accommodation by the lens. The rectus superior rotates the bulb upward and somewhat inward, the rectus medialis inward, the rectus inferior downward and somewhat inward, the obliquus inferior upward and outward. With paralysis: ptosis, the paralyzed eye deviates outward, diplopia (upon raising the lids), dilatation and loss of the pupillary reaction, disturbances of accommodation.

Trochlearis supplies the M. obliquus superior. This rotates the bulb downward and outward. With paralysis homonomous oblique double vision upon looking down.

Trigeminus; the **motor** portion supplies the jaw muscles: Mm. masseter, temporalis, pterygoidei, myohyoideus and the anterior belly of the digastric. The **sensory** portion supplies the skin of the face and of the head back to the ears, specifically, the first branch passes to the skin of the forehead and scalp up to the vertex, the upper eyelids and the bridge of the nose, the second branch to the upper lip and the upper half of the cheeks, the third branch to the lower half of the cheek and the skin over the temporal bone and the chin. In addition the trigeminus supplies sensory fibers to the cornea and conjunctiva; with a lesion of this nerve (e.g., with a tumor in the pontine angle) the cornea of the eye on that side is anæsthetic and the corneal reflex absent (see page 437). The trigeminus also innervates the dura mater, as well as the mucous membranes of the mouth, nose and pharynx, with sensory fibers. With a lesion of the 5th nerve the patient is unable to feel food in that half of the mouth and the nasal mucous membrane may be tickled with a feather without causing the patient to sneeze. The lingual branch is the nerve of taste for the anterior two-thirds of the tongue. The taste fibers arise from the chorda tympani which leaves the facial nerve between the geniculate ganglion and the stylomastoid foramen, and passes in an arch through the tympanic cavity to join with the lingualis after its exit from the fissura glaseri.

Abducens supplies the M. rectus lateralis; with paralysis the eye cannot be moved outward, the paralyzed eye deviates inward and there results uncrossed diplopia when the glance is directed toward the side of the lesion; upon looking toward the sound side there is no diplopia.

Facialis supplies all the muscles of the face with the exception of the stylohyoideus and the posterior belly of the digastric. With paralysis of the facial nerve the affected side of the face is immobile; the naso-labial fold on that side is obliterated; the forehead cannot be wrinkled nor the eye closed and the lips cannot be moved. The relation of the M. facialis to the chorda tympani explains the fact that, with a lesion between the geniculate ganglion and the point of offset of the chorda tympani, there appear disturbances of the sense of taste in the anterior two-thirds of the tongue and reduction

in the secretion of saliva. With **central** paralysis of the facial muscles (e.g., with hæmorrhage in the internal capsule), usually only the lower half of the face is paralyzed; with **peripheral** paralysis (e.g., with destruction of the petrous portion of the temporal bone) the upper half is also paralyzed and reaction of degeneration is present.

Acusticus: Test hearing and make otoscopic examination. The semicircular canals, in the petrous portion of the temporal bone, are the sensory organs for orientation in the three dimensions of space and are particularly important in the maintenance of equilibrium. The portion of the 8th nerve arising in the semicircular canals is distinguished as the vestibular nerve in contrast to that arising from the cochlea, the auditory nerve proper, N. cochlearis. The latter passes to the acustic nucleus in the medulla and thence, through the posterior corpora quadrigemina, to the medial geniculate body and the temporal lobe (see page 384). The vestibular nerve passes to the vestibular nucleus in the medulla and, through Deiter's nucleus, for the most part to the cerebellum. For the details of testing the hearing and the function of the vestibular apparatus see pages 471–474.

Glossopharyngeus supplies taste and sensory fibers to the posterior third of the tongue as well as the pharynx. It is tested by applying quinine, sugar, salt, or vinegar to the posterior third of the outstretched tongue; it is best to hold before the patient a table enumerating the various qualities of taste: Bitter, sweet, salt and sour, and to direct him to point thereat with the finger. It is not certain whether the N. glossopharyngeus also carries motor fibers to certain pharyngeal muscles.

Vagus supplies the pharynx, larynx, œsophagus, heart, aorta and stomach with sensory fibers, and transmits fibers to the viscera of the thorax and abdomen. Stimulation of the vagus causes slowing of the pulse; paralysis: Acceleration of the pulse and slowing of the respiration. Fibers also pass in the vagus which provide sensory and motor innervation to the muscles of the palate, pharynx, larynx, and œsophagus. With paralysis of these fibers there results paralysis of the palate and pharynx, nasal speech, dysphagia,

dysphonia and cadaver position of the vocal cords as well as loss of sensibility and of reflexes of the larynx.

Accessorius supplies the M. sternocleidomastoideus and the greater proportion of the trapezius. The M. sternocleidomastoideus draws the mastoid process towards the sternum and the chin toward the opposite side. The M. trapezius raises the scapula and particularly the acromion. With paralysis the acromion and the arm sink downward and there is difficulty in raising the shoulder.

Hypoglossus, motor nerve to the tongue (Mm. genio-, hyo-, stylo-glossus, internal muscles of the tongue; M. genio-, omo-, sterno-hyoideus, hyo-, and sterno-thyreoideus). With paralysis of the hypoglossus the tongue deviates toward the paralyzed side upon contraction of the Mm. genio-glossus and stylo-glossus of the sound side. With peripheral paralysis the affected half of the tongue atrophies.

Concerning the position of the cranial nerves, together with their derivation from the brain stem and medulla, see figures 115–126.

Spinal Nerves

Plexus cervicalis (C1–C4)—sensory to skin from occiput behind the ears, over the neck and shoulders down to clavicles; motor to deep muscles of neck and to Mm. scaleni. **N. phrenicus,** motor nerve to diaphragm, arises from C4. N. occipitalis major carries sensory supply from back of the head up to vertex; its pressure point lies just behind the proc. mastoideus. N. occipitalis minor supplies sensory fibers to a strip just behind the ear, and N. auricularis magnus to the pinna, the angle of the jaw and side of the neck.

Plexus brachialis (C5–8, Th. 1–2). With a lesion of the 5th cervical root (see Fig. 145) there results motor paralysis of Mm. deltoideus, biceps, brachial intern., brachioradialis and infraspinatus (**Erb's paralysis**).

N. thoracalis longus: M. serratus anterior; fixes and rotates scapula and raises acromion; in case of paralysis arm cannot be raised above the horizontal. If the arm be extended forward the inner border of the scapula is drawn away from the ribs and stands out like a wing.

Nn. thoracalis anteriores supply the Mm. pectoralis major and minor; the pectoralis maj. adducts the arm and draws it forward (e.g., in striking a blow).

N. dorsalis scapulæ: Mm. rhomboidei (draw scapula upward and inward and assist serratus). Mm. levator scapulæ and serratus posterior superior.

N. suprascapularis: M. supraspinatus, fixes the head of the humerus in the shoulder joint, rotates the arm outward and acts with the deltoid in raising the arm. M. infraspinatus rotates the upper arm outward, e.g., in sewing.

N. subscapularis: M. subscapularis rotates the upper arm inward. Mm. teres major and latissimus dorsi: draw the upper

FIG. 141.

FIG. 142.

arm toward the body and posteriorly (e.g., in placing hand on sacrum) lower and adduct the scapula.

N. axillaris: M. deltoideus raises the arm to the horizontal (elevation of the arm above the horizontal is accomplished through rotation of the scapula by means of M. serratus anterior); with paralysis of the deltoid the arm hangs limp against the body. M. teres minor assists M. infraspinatus. Sensory supply to axilla, see Figs. 134 and 135.

N. cutaneous brachii medialis: Skin of inner surface of upper arm; see Figs. 141 and 142.

N. cutaneous antibrachii medialis: Skin of medial (ulnar) surface of forearm. (In Figs. 141 and 142 abbreviated as cut. medius.)

N. musculocutaneous: Mm. biceps and brachialis internus, flex the forearm; the former acts at the same time to supinate the flexed forearm. M. coracobrachialis draws the raised arm downward. Sensory fibers: N. cutaneous antibrachii lateralis (in Figs. 141 and 142 abbreviated to cut. lateral).

N. medianus: Mm. flexor carpi radialis, pronator teres and quadratus, flexor digitorum communis superficialis (flexes 2nd phalanges) and the radial half of the flexor digitorum profundus (flexes 3rd phalanges). M. palmaris longus, Mm. flexor pollicis longus and brevis (flex 2nd and 1st phalanges), abductor brevis and opponens pollicis oppose and draw the thumb into palm. (Sensory fibers, see Figs. 141 and 142.)

With **median nerve palsy** pronation and flexion of the hand are almost entirely lost; flexion and opposition of thumb impossible. Patient cannot touch tip of extended little finger with tip of extended thumb but both fingers are flexed in the attempt. Flexion of both terminal phalanges lost but basal phalanges can be flexed by Mm. interossei. Patient cannot hold fast to objects with first three fingers and is unable, therefore, to write or to sew, but can grasp tightly with fourth and fifth fingers whose flexor profundus is in part supplied by the N. ulnaris. Atrophy of the muscles composing the thenar eminence.

N. ulnaris: Mm. flexor carpi ulnaris, flexor digitor. comm. profundus for last two fingers. Mm. interossei and lumbricales which flex the first phalanges and extend the last; Mm. interossei volares draw the fingers together, the dorsales spread them apart. M. adductor pollicis approximates the metacarpus of the thumb to that of the index finger. Sensory fibers, see Figs. 141 and 142.

With **ulnar paralysis** flexion and ulnar deviation of the hand as well as flexion of the last two fingers are impaired. Motion of little finger lost, as are also flexion of basal, and

extension of terminal phalanges of last four fingers. With long-standing paralysis; claw-hand: basal phalanges flexed dorsalward, middle and terminal phalanges volarward, atrophy of interossei, adductor pollicis and hypothenar eminence.

N. radialis—extensors of arm, hand and fingers; M. triceps extends the forearm; M. brachioradialis, flexes the forearm; M. supinator, supinates the extended forearm; M. extensor carpi radialis longus and brevis, M. extensor carpi ulnaris (extensors of wrist), Mm. extensor digitorum communis, extensor indicis and digiti quinti (extend basal phalanges), M. extensor pollicis longus (moves 1st phalanx), M. abductor pollicis longus (abducts thumb)—cutaneous branches, see Figs. 141 and 142. Cutaneus brachii posterior (= Cut. br. post. and sup.); posterior and outer surface of forearm; cutaneus antibrachii dorsalis (= cut. post. inferior): dorsal surface of forearm and radial side of hand.

Radial paralysis: The hand hangs limply from the wrist, the fingers slightly flexed; inability to extend hand or fingers, and to abduct or extend the thumb. Extended arm cannot be supinated (with arm bent, forearm may be supinated by biceps). If the triceps is also involved forearm cannot be extended. **Lead palsy** produces a similar picture except that the triceps and brachioradialis are usually spared. The sensory disturbances associated with lesions of the arm nerves are shown in the accompanying figures; they are usually less pronounced than the motor paralyses, and, with lead poisoning, rarely occur.

Thoracic nerves—skin of thorax and abdomen—intercostal and abdominal muscles.

Plexus lumbalis (Th. 12, L. 1–4). The posterior branches supply the M. erector trunci = sacrospinalis, and skin of upper gluteal region. The anterior sensory branches; Nn. iliohypogastricus, ilioinguinalis, lumboinguinalis, spermaticus externus and cutaneus femoris lateralis, supply the skin over the hips, mons veneris and the anterior and lateral aspects of the upper half of the thighs.

N. femoralis: M. iliopsoas (flexes hip), M. quadriceps femoris (extends lower leg), M. sartorius; sensory branches: anterior aspect of thigh and knee, inner aspect of lower leg.

N. obturatorius: Mm. obturator ext., pectineus, adductores magnus, longus and brevis, M. gracilis (adducts thigh, e.g., in crossing one knee over the other). Sensory branches to inner side of thigh.

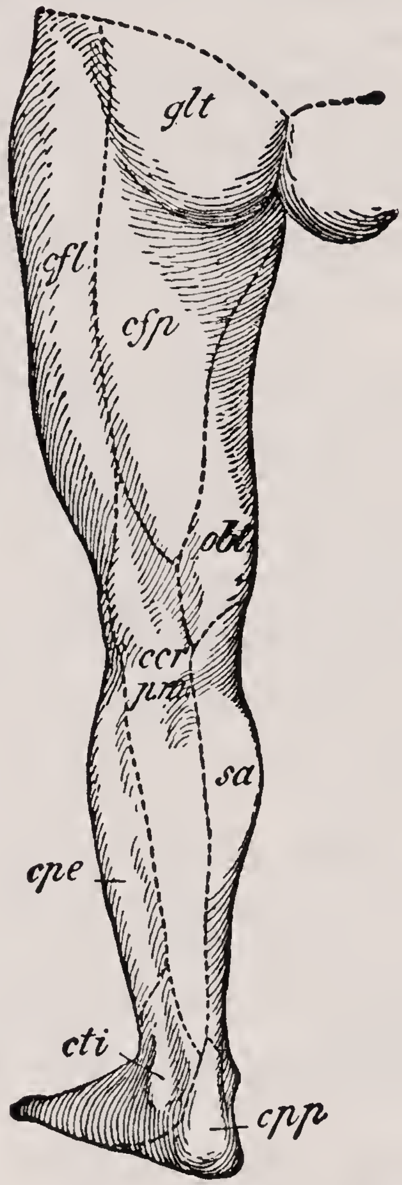


FIG. 143.

cfl = *cutaneus femoris lateralis*
cfp = *cutaneus femoris posterior*
glt = *gluteal branches of cut. fem. post.*
cpe = *communicans peronei* = *suralis*
obt = *obturatorius*
ccr. p. m. = *cutaneus cruris posterior medius*
cpp = *cutaneus plantaris proprius*
sa = *saphenus*
cti = *communicans tibialis* = *suralis*

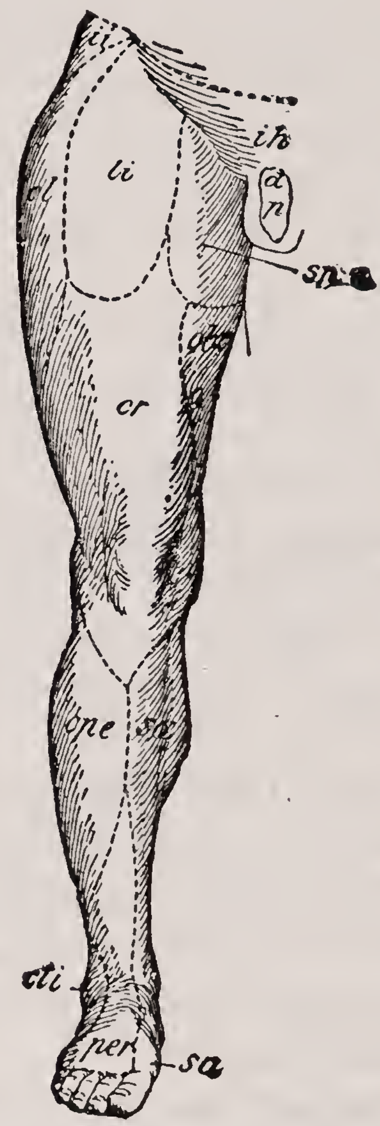


FIG. 144.

ii = *ilioinguinalis*
li = *lumboinguinalis*
sp. e. = *spermaticus externus*
ih = *iliohypogastricus*
dp = *dorsalis penis*
cl = *cutaneus femoris lateralis*
cr = *femoralis (cruralis)*
per = *peroneus*

Plexus sacralis (L5, S1–5) supplies the bladder, rectum, genitalia, perineum and nates with motor and sensory fibers.

N. glutæus superior: Mm. glutæus medius and minimus, abduct the leg or, with the leg fixed, bend the trunk to the side; in walking these muscles fix the pelvis, holding the trunk

upright and preventing the pelvis from falling toward the side of the swinging leg. With paralysis the pelvis sinks toward the sound side and the trunk toward the paralyzed side; with bilateral paralysis gait is waddling. M. pyriformis rotates the leg outward. M. tensor fasciæ latæ flexes thigh and rotates it inward.

N. glutæus inferior: M. glutæus maximus, powerful extensor of thigh, e.g., in climbing stairs or jumping.

N. cutaneus femoris posterior: skin of lower part of buttock and posterior surface of thigh.

N. ischiadicus: Skin of lower leg and foot except for that supplied by N. saphenus. External rotators of the thigh: Mm. genelli, obturator int. quadratus femoris. Mm. biceps femoris, semitendinosus and semimembranosus (flex lower leg on knee). N. ischiadicus divides in mid-portion of thigh into N. peroneus and N. tibialis.

N. peroneus (chiefly composed of fibers from 5th lumbar root) supplies the skin of the outer and posterior aspects of the lower leg and the back of the foot, as well as the M. tibialis anterior (raises the foot, particularly the medial side thereof). Mm. extensor digitor. longus, extensor hallucis longus, Mm. peronei (raise the foot, particularly its outer side).

With **peroneus paralysis** the foot hangs (toe-drop), the toe scrapes in walking, making it necessary to raise the knee sharply with each step (**steppage gait**).

N. tibialis supplies the skin of the sole and outer side of the foot and malleolus, and the muscles of the calf: Mm. gastrocnemius and soleus (extend the foot by means of the Achilles tendon); M. tibialis posterior (adducts the foot and raises its inner border); Mm. flexor digitorum longus and brevis, flexor hallucis longus and brevis, as well as the muscles of the sole of the foot.

With **tibialis paralysis** inability to extend foot plantarward; to stand on toes or jump.

N. pudendus internus supplies skin of perineum, the labiæ or penis and scrotum (but not the testis or spermatic cord which are supplied from the 2nd lumbar segment), the mucous membrane of the urethra and vagina, the muscles of the floor of the pelvis, and the striated Mm. compressor urethræ and sphincter ani externi.

Spinal Cord Segments and Corresponding Roots	Muscles and Corresponding Functions	Sensory Distribution	Reflexes
1st Cervical Segment.	Small cervical muscles. **Rotation and backward bending of the head.**	Neck and back of head.	
2nd and 3rd Cervicals S.	Neck muscles. Trapezius. **Forward bending of the head. Elevation of the shoulders.**	Back of head and outer lateral surface of neck.	
4th Cervical S.	Scaleni. Diaphragm (N. phrenicus). Levator scapuli. Rhomboids and supra- and infraspinati. **Inspiration and outward rotation of the upper arm.**	Neck, shoulder and breast as far as the 2nd rib and spine of the scapula.	
5th Cervical S.	Deltoid. Biceps. Coracobrachialis. Brachialis internus. Brachio-radialis. Supinator. Supra- and infraspinati. **Elevation (abduction) of the upper arm. Flexion and supination of the forearm.**	Dorsal aspect of shoulder and arm —outer aspect of upper arm.	Biceps. Tendon reflex.
6th Cervical S.	Pectoralis major and minor. Latissimus dorsi and teres major subscapularis. Servatus anterior.	Outer aspect of the upper arm and radial side of the forearm.	Triceps. Tendon reflex.

Spinal Cord Segments and Corresponding Roots	Muscles and Corresponding Functions	Sensory Distribution	Reflexes
	Pronators of the forearm. Triceps. **Adduction and internal rotation of upper arm.** **Extension and pronation of the forearm.**		
7th Cervical S.	Extensors of wrist and fingers. Flexors of wrist. **Flexion and extension of the wrist.**	Radial side of forearm and thumb.	Tendon reflexes in the forearm and hand.
8th Cervical S.	Long extensors and long flexors of the fingers. Thenar muscles.	Middle of forearm and middle of the hand (palmar, volar) on flexor and extensor surfaces.	
1st Thoracic S.	Small muscles of the hand and fingers. (Interossei, thenar and hypothenar.) 8C and 1D. **Movements of the thumb and fingers.**	1st and 2nd **thoracic segments.** Inner aspect (ulnar) of the upper arm, forearm and little finger.	C8–D9 Dilatation of the pupil through the sympathetic.
2nd–6th Thoracic S.	Spinal muscles. Intercostal muscles	2nd–4th **thoracic segments.** Skin of back from 7th cervical vertebra and spine of scapula to the 5th thoracic vertebra. Skin of breast from 2nd rib to height of nipple.	Sympathetic to heart C8–D4. Sympathetic of stomach, duodenum and jejunum. D6–D8

Spinal Cord Segments and Corresponding Roots	Muscles and Corresponding Functions	Sensory Distribution	Reflexes
	Spinal and abdominal muscles.	5th and 6th **thoracic segment.** Back from 5th–8th thoracic. Skin of breast from nipple to the 7th rib.	Gall bladder Th. 9–10. Colon-Th. 11–12.
7th Thoracic S. 1st Lumbar S.		7th–9th **thoracic segment.** Skin of back from 8th–12th thoracic vertebra. Skin of the abdomen from 7th rib— the umbilicus.	Upper abdominal superficial reflex 8–9 Th.
		10th–12th **thoracic segment.** Lumbar region from 12th thoracic vertebra to 5th Lumbar. Skin of the abdomen from the umbilicus to Poupart's ligament.	Lower abdominal superficial reflex 10–12 Th.
1st Lumbar S.	Lower abdominal muscles. Quadratus lumborum. Sartorius. Psoas.	Outer aspect of gluteal region. Inguinal region.	Sympathetics of urinary bladder. L1.
2nd Lumbar S.	Iliopsoas-cremaster.	Outer side of the thigh. Sensory fibers to the testes and vas.	1–3 L. Cremasteric reflex.
3rd Lumbar S.	Iliopsoas. Adductors of the thigh. Quadriceps. Internal rotators of the thigh.	Anterior and inner aspect of the thigh and knee.	2–4 L. Patellar tendon reflex.

Spinal Cord Segments and Corresponding Roots	Muscles and Corresponding Functions	Sensory Distribution	Reflexes
	2nd and 3rd Lumbar: **Flexion internal rotation and abduction thigh.**		
4th Lumbar S.	Extensor cruris quadriceps. **Extension of the leg.**	Inner aspect of the leg and foot. Anterior aspect of the thigh.	4–5 L. Gluteal reflex.
5th Lumbar S.	Gluteus medius and minimus. Semimembranosus and semitendinosus. Biceps femoris. Tensor fasciæ latæ. Tibialis anterior. **Abduction of the thigh. Flexion of the leg.**	Outer aspects of the leg and foot. Outer aspect of the thigh.	
1st Sacral S. External rotators of the thigh.	Gluteus maximus L4–S2. Pyriformis obturator int. Gemelli Quadratus femor Extensors (dorsiflexors) of the foot. Tibialis ant. Peronei. Extensor digitor. comm. **Extension and external rotation of the thigh. Dorsal flexion of the foot and toes.**	Posterior aspects of the thigh. Posterior aspect of the calf. Sole of the foot. Outer border of the foot. Toes.	Plantar reflex. Achilles reflex. L2–L4.
2nd Sacral S.	Large calf muscles (gastrocnemius, soleus).	Seat and posterior surface of the thigh (saddle anæsthesia).	Achilles tendon reflex. Erection.

Spinal Cord Segments and Corresponding Roots	Muscles and Corresponding Functions	Sensory Distribution	Reflexes
	Extensors and flexors digitor. comm. l. et. hallucis l. Tibialis posterior. Small muscles of foot. **Plantar flexion of the foot. Bending of the toes. Erection.**	Outer aspect of the leg and outer border of the foot. Sensory fibers to the bladder and rectum.	
3rd Sacral S.	Perineal muscles. Cross striated musculature of the urinary bladder, rectum and genital organs. **Voluntary starting of urination and defecation.**	Medial part of the seat—perineum, scrotum and penis.	Ejaculation. Bladder and rectum S2–S5.
4th and 5th Sacral and Coccygeal S.	**Voluntary starting of urination and defecation.**	Neighborhood of the buttocks, perineum, anus.	Anal reflex.

GENERAL SYMPTOMS

Disturbances of **consciousness** occur with various types of disease of the brain, among others with any abnormal increase in intracranial pressure, with apoplexy, during epileptic convulsions, with brain tumor or meningitis, and occasionally, though rarely, with hysteria. One distinguishes between **apathy,** and **semi-stupor,** i.e., a condition between sleeping and waking which may be complicated by **delirium.** Pathological drowsiness is designated as **somnolence;** if it be possible to arouse the patient only by vigorous stimulation the condition is called **sopor. Coma** is a state of total loss of consciousness, from which the patient cannot be aroused, and in which reflexes (corneal and pupillary) may be lost.

Disturbances of consciousness are present in many severe infectious diseases, e.g., in typhoid, and also with certain

intoxications, with nephritis and diabetes (uræmic and diabetic coma), as well as with profound exhaustion from a variety of causes.

Disturbances of **intelligence**: If all mental and intellectual processes are depressed one speaks of **feeble-mindedness**; if this be present in a conspicuous degree the condition is called **imbecility.** If this impairment be congenital it is called **idiocy.** Such a condition, associated with hypo-function of the thyroid due either to maldevelopment or to goiter, is characteristic of **cretinism**; this is also distinguished by retarded development, which is particularly pronounced in the skeletal system, a peculiar, bloated appearance of the face and soft parts, and occasionally, by partial or complete deafness.

Defects of memory are commonly present to a certain degree in old age; conspicuously defective memory is often a sign of cerebral disease involving the cortex. **Amnesia,** in which loss of memory is transient, is not to be confused with such defects. This is present in many acute and severe diseases and is particularly associated with epileptic attacks and their equivalents. **Attentiveness** is the ability to retain in memory freshly made impressions and to reproduce them, e.g., to repeat a long sentence or series of numbers. This is impaired in many diseases of the central nervous system and particularly in dementia paralytica. **Korsakoff's syndrome** is characterized by a loss of memory for recent events, while events in the more distant past are recalled with accuracy. This type of amnesia is frequently associated with chronic alcoholism.

Speech may be altered in a characteristic fashion with various mental diseases; slow or sad in depression; excited and loud in various pathological types of elation and mania. **Euphoria** is met with in general paresis, chronic alcoholism, and occasionally in multiple sclerosis. **Moral defects** may appear with many diseases of the central nervous system (tumors, degeneration of the cortex), with chronic forms of intoxication (alcohol, morphine or cocaine), and in certain mental diseases, e.g., in dementia paralytica.

Delusions are false opinions which may either develop spontaneously or as a result of hallucinations or illusions.

Headache is present in a variety of abnormal conditions: In many infectious diseases and particularly at the onset (e.g., with typhoid, meningitis, and influenza), in many types of intoxications (alcohol), with gastro-intestinal disturbance and particularly with constipation, with anæmia, cardiac disease, and with acute and chronic inflammation of the nasal sinuses. **Migraine** is a condition characterized by the development of terrific headaches at irregular intervals, characteristically limited to one-half of the head (**hemicrania**) and associated with vomiting, indigestion and sometimes with transient disturbances of vision (scintillating scotoma). Regularly occurring, daily headaches, often limited to one half of the forehead or occiput, are present in malaria and relieved by quinine. Severe and protracted headache is never an insignificant symptom; such is often present in nephritis. With diseases of the brain headaches are not always present but with affection of the meninges they are rarely absent: purulent or tuberculous meningitis, pachymeningitis hæmorrhagica, and syphilitic meningitis. Headache is an almost constant accompaniment of brain tumors and of such other conditions as are associated with increased intracranial pressure.

Increased intracranial pressure is accompanied by headache, projectile vomiting, bradycardia, stupor or coma and, when it is protracted, by choked-disc. Lumbar puncture under these conditions shows a conspicuous increase in the spinal fluid pressure, but only in cases in which there is free communication between the cerebral ventricles and the subarachnoid space of the spinal cord.

Those symptoms which are not occasioned by organic disease of the nervous system are designated as **functional disturbances** while those which have pathological basis in demonstrable nervous system disease are known as **organic.** The symptoms which are due to localized disease of the brain will be mentioned below.

The **functions** of the nervous system as well as of the nerves are divided into (1) **sensory** or centripetal, (2) **motor** or centrifugal, and (3) an apparatus which represents a connecting link between the sensory and motor functions, known as the **reflex** apparatus. Sensory functions are those which

are derived from the higher organs of sense, e.g., the eye, ear, and olfactory organs as well as the vestibular apparatus.

SENSORY FUNCTION

Among the sensory nervous functions one may differentiate those which provide an impression of the outer world, to which belong sight and hearing (**exteroceptive** impressions), and those which convey impulses having to do with various body processes (**proprioceptive** impulses), e.g., the tension of muscles and tendons, sense of position, and particularly impulses from the viscera (heart, lungs and intestines). The proprioceptive impulses from the internal organs, for the most part, never reach consciousness; they do, however, bring about appropriate reflex phenomena.

Among the sensory functions one distinguishes further **superficial sensibility**, which is mediated by the nerves to the skin, and **deep sensibility** consisting of impulses from the muscles, joints, tendons and bones. These various sensory impulses are all carried in the mixed nerves which supply, as well, the motor fibers to the muscles.

The **superficial sensibility**, i.e., that of the skin and mucous membranes, provides sensations of touch (pressure), pain and temperature; it makes possible the accurate localization of the point of stimulation and, in addition, the distinction of single or multiple stimuli (simultaneous stimulation at two points). Over the tips of the fingers the acuity of touch is much greater than over the back or extremities; thus stimulation at two points not greater than 4 mm. apart may be distinguished on the finger tips whereas over the back such points must be far wider apart.

Magnus Blix, Goldscheider and M. von Frey have demonstrated a sharply localized end apparatus in the skin which acts in a specific fashion to afford perception of touch, heat or cold. Sensation of heat and cold is derived from separate end organs, whose indifferent point is approximately that of the body temperature. At certain points upon the skin there seems to be relatively increased sensibility to pain but these "pain points" are by no means so sharply circumscribed and specific as those for heat, cold, and pressure. The specific nerve endings are distributed over the skin but in not extremely great

numbers per square cm. The most sensitive points of the skin seem to be about the base of the hairs covering the greater portion of the body surface and also over the hair-free areas, the palms and soles. Since the demonstration of the function of the various nerve endings in the skin requires far too much time, it is sufficient, in a clinical examination, to test for the sense of **touch** in a rather gross fashion by stroking the skin with a brush or bit of cotton, and for **pain** by touching the skin alternately with a sharp or dull point. The pain sense may be more accurately and quantitatively studied with the faradic apparatus: A metal brush electrode is placed upon the skin and the sensitivity is tested relative to the current strength which is required to produce sensation. In certain diseases, e.g., tabes dorsalis, the **conduction of pain sense** is apparently delayed while that of touch is unimpaired. Such individuals may recognize the prick of the needle first as touch and only several seconds later as pain. In the same diseases it is sometimes necessary to repeat stimulation in order to produce sensation (summation of stimuli).

Temperature sense is examined by touching the skin with the base of a test tube filled with warm or cold water. One should also test the ability of the patient to **localize** such stimuli. During a sensory examination the eyes of the patient should of course be covered and his attention held as closely as possible.

If such an examination shows a complete insensibility one speaks of **anæsthesia;** a pathological diminution of sensation is known as **hypæsthesia,** and such patients often complain of a subjective sensation as though everything were covered with cotton wool. **Hyperæsthesia** is a condition in which the minimal stimulus brings about an increased or even maximum sensation; one speaks of **paræsthesia** when the quality of the stimulus is falsely interpreted.

Head showed that, upon section of cutaneous nerves in his own arm, the sensation of the skin was entirely lost. **Deep sensibility,** however, remained entirely intact and pressure upon the muscles or bones was not only perceived but sometimes interpreted as a pain which could be relatively sharply localized.

The state of contraction of the **muscles** is apparently

transmitted by end organs in the muscles themselves, "the neuro-muscular bundles." Sensation from the **bones** is limited to the perception of pain and pressure and, most important, of vibration, tested by placing a vibrating tuning fork directly against some bony prominence (pallæsthesia). The sensory nerves of muscles, tendons and joints, together with those from the skin, afford accurate perception of position and movements of the extremities and joints. They furnish, as well, an indefinite sense of the degree of muscular effort.

The **deep sensibility is tested** by asking the patient to differentiate, in the first place, between light touch and deep pressure upon the skin or to evaluate a weight placed upon the skin. It is further tested by passively moving certain joints (fingers or toes) and demanding that the patient either describe or reproduce these movements.

With severe abnormalities of deep sensibility the patient may be entirely disoriented as to the position of his extremities, and totally unable to interpret passive movements. Such a patient is unable to find one hand with the other, and cannot tell whether his legs are flexed or extended.

Deep sensibility, and particularly that of the bones, tends to be conspicuously decreased in **tabes.** It is this disturbance which leads to the uncertainty of movement, and, thereby, to the ataxia characteristic of this disease. If the position of the feet and joints and the condition of the contraction of the muscles of the lower extremities can no longer be perceived with the normal accuracy the patient, upon attempting to stand with the eyes closed, sways and tends to fall. One tests for this **Romberg's phenomenon** by directing the patient to stand with the feet parallel and close together, and to close the eyes. As long as the eyes are closed the patient cannot retain his balance, but upon opening the eyes he is able to control his station more or less perfectly.

The facts that, under pathological conditions, there is sometimes a disturbance of deep sensibility without impairment of the sensation from the skin or vice versa, and that, among the disturbances of cutaneous sensation, the perception of pain and temperature may be lost without impairment of the sense of touch, indicate that these various sensory

functions are transmitted through separate paths in the spinal cord.

With complete section of a peripheral nerve, e.g., the radial or sciatic, or with transverse section of the spinal cord, all sensory impressions from the domain of the severed nerve are cut off from the brain, and therefore from consciousness, and there results complete anæsthesia in this region. With **hemisection** of the spinal cord there is motor paralysis upon the affected side, the tendon reflexes are accentuated and deep sensibility is tremendously depressed. The **paths of deep sensibility** must therefore pass upward upon the **same side of the cord**: it is further to be assumed, from other experimental sections, that they travel in the **posterior columns.** On the opposite side (at least for a few segments below the lesion) there is a striking depression of the sense of pain and temperature. From these facts one concludes that the nerve fibers bearing sensory impulses of **pain and temperature** cross to the opposite side soon after their incorporation in the spinal cord and travel upward in the **anterior column** (a fact which is born out by experimental evidence). The **sense of touch,** in cases of hemisection of the cord, tends to be impaired somewhat on both sides but more strikingly so upon that opposite the lesion, indicating that these sensory paths are in part crossed, and in part uncrossed. In **syringomyelia** the central portion of the cord is destroyed for a certain distance about the central canal. It is characteristic of this disease that, in the region of the lesion, the sense of pain and temperature is conspicuously impaired or sometimes absent, so that the patient perceives burns, injuries and operations in the area supplied by the segments involved, not as pain, but simply as touch. This **dissociation** of sensation forces the conclusion that the tracts for **pain and temperature** cross the mid-line in the gray substance **near the central canal.**

The posterior columns of the cord, which carry the fibers of deep sensibility and in part also those of touch, degenerate upward upon section, and this degeneration may be followed up to the appropriate nuclei in the medulla. From these medullary ganglion cells there arise secondary neurones which soon cross the mid-line in the decussation, and, together with sensory tracts, which have crossed lower down and have

passed upward in the antero-lateral columns, course in the **median lemniscus,** through the medulla, to the **optic thalamus.** Here begins a third sensory neurone which passes upward through the posterior limb of the internal capsule to end in the cortex of the parietal lobe. **Lesions,** therefore, involving the **median lemniscus** produce severe disturbances of all sensations (**hemianæsthesia**), and ataxia, upon the **opposite side.** Localized disease in the thalamus leads to sensory disturbances upon the entire opposite half of the body, and is not infrequently associated with painful paræsthesiæ, also upon the opposite side. From the nuclei of the thalamus fibers pass to the lenticular nucleus which carry impulses important to the reflex control of coördination of movement.

Since the sensory paths from the thalamus, having passed through the internal capsule, are distributed in a fan over a wide area of the parietal cortex, **circumscribed lesions** in the **corona radiata** may lead to isolated disturbances of sensation in **limited areas,** e.g., in a hand, in a single finger, or in an entire extremity. With disease of the **cortex** isolated disturbances, e.g., of deep sensibility, may develop and, indeed, such may result from lesions in front of, or behind the ascending frontal convolution, since the motor functions of the former area are always indirectly connected with those of the latter through the paths of proprioceptive sensibility. Disturbances of touch are inconstant with cortical lesions and their accurate demonstration is usually complicated by the patient's inability to concentrate. With cortical lesions in the parietal region there are often **defects of memory** and **association.** Patients with such lesions are sometimes unable to distinguish between various previously familiar objects. It is, therefore, to be assumed that, in the parietal cortex the various sensations are woven into an image which is then compared with previous similar, and usually visual, impressions (**stereognosis**).

The disturbance of sensibility occasioned by lesions of the **peripheral nerve** is limited to the area of skin supplied by the nerve in question (see diagram of the area supplied by various cutaneous nerves upon pages 405 and 406) but this disturbance usually involves an area somewhat smaller than the actual domain of that nerve, since the supply to adjacent

areas of skin is somewhat overlapped. With disease of the **spinal cord,** e.g., tabes, myelitis or compression, the sensory disturbances correspond to the segments of the cord from which the nerves to these areas arise and not to the domain of any particular peripheral nerve (cf. figures 133 and 134). With localized **cerebral lesions** (hæmorrhage or softening in the sensory cortex, internal capsule, or thalamus) sensory disturbances are limited to one-half of the body (hemihypæsthesia) or even to a single limb, in which case the distal portions (e.g., hands and fingers), are involved to a greater degree than the proximal; it should be said, however, that, with localized cerebral disease, sensory disturbances are sometimes of a "radicular type." Again with cerebral disease, particularly when it involves the cortex, the stereognostic sense and that of localization are usually altered to a greater degree than the sense of touch or temperature, and these more strikingly than that of pain. With **hysteria** there may be also hemianæsthesia, or disturbance of sensation in a single extremity (psychogenic disturbances of sensibility); these **functional** disturbances of sensation are distinguished from those occasioned by **organic** lesions by their greater intensity, and by the fact that their arrangement corresponds to no anatomical distribution of nerve fibers, roots or segments.

SENSORY SYMPTOMS

Among these are sensations of tingling, itching, burning and formication, all of which are described as **paræsthesiæ.** To this group belong also certain abnormal sensations of pain.

With disease of the peripheral nerves, e.g., alcoholic or post-diphtheritic neuritis, it sometimes happens that the sensibility to external stimuli (touch, pressure, temperature and muscle sense) is entirely lost in the affected area although the patients complain of severe pain referred to this area. This "anæsthesia dolorosa" is explained by the fact that pain arising in the diseased nerve trunk is referred to the end apparatus. **Neuralgia** is characterized by pain localized in a definite neurological area, and usually following the course of a nerve trunk. These attacks are sometimes paroxysmal, particularly in cases of neuralgia of the trigeminus, or, as is most frequently the case in sciatica, may be characterized

by continual pain. In neuralgia the affected nerve trunk is usually tender to pressure along its course, and especially at those points where it crosses over the bones. Such "pain points" are (1) with neuralgia of the 1st branch of the trigeminus, in the middle of the supraorbital ridge, (2) with neuralgia of the 2nd or 3rd trigeminal branches, over the infraorbital and mental foramina, (3) with intercostal neuralgia, next the spinal column, in the mid-point of the nerve or adjacent to the sternum, and (4) with sciatica, over the sacro-iliac symphysis, over the greater sciatic foramen, in the popliteal space, over the head of the fibula or behind the maleolæ. Characteristic of sciatica is the **Lasegue's phenomenon:** With the thigh flexed extension of the knee is accompanied by pain, due to stretching of the nerve. The ankle-jerks are often absent with sciatica.

A similar sign (pain upon extending the knee upon the flexed thigh) is encountered with cases of meningitis and is then known as **Kernig's** sign. It is also of diagnostic importance that a patient with meningitis can rarely sit upright in bed without bending the knees.

Disease of the posterior roots of the spinal cord (e.g., with compression from tumors or caries), is accompanied by terrific pains which are referred along the course of the nerves (root pains). With **tabes dorsalis** there occur **lightning-like,** lancinating pains which spread rapidly to one or more extremities (usually the legs). In this disease there may also appear so-called **girdle sensations,** a feeling of constricting pressure in the lower thoracic or upper lumbar region; here also the skin over the trunk is so hyperæsthetic that the mere touch of a cold object elicits excessive pain.

Head's-zones are circumscribed cutaneous areas, hypersensitive to light touch or squeezing, which are found with various diseases of the viscera. These zones characteristically occur in those cutaneous areas whose sensory supply is derived from the same spinal cord segment as that (sympathetic) of the particular organ or organs involved. In such regions there is sometimes not only hyperæsthesia but referred, seemingly spontaneous, pain, e.g., with aortic or coronary disease in the lower side of the neck, along the inner surface of the left (and more rarely the right) arm, and in the

5th and 6th thoracic segments; with gastric ulcer in the 8th and 9th thoracic segments; with gall-bladder colic in the 6th to the 9th right thoracic segments, radiating to the shoulder blade; with renal colic in the 10th and 11th dorsal segments on the affected side, radiating to the symphysis and groin.

REFLEXES

The impulses transmitted from the peripheral end-organs via the sensory nerves, i.e., from the skin, tendons, bones, sense organs and viscera, act upon certain centers, in the spinal cord, to stimulate the motor apparatus. Such stimuli set up impulses which are transmitted through the motor nerves to their end-organs, into the smooth and striated musculature, and the glands. The entire process is known as a reflex. The transmission of sensory impressions to the motor ganglion cells of the reflex center may occur either directly, through collateral branches of the sensory nerves, or, more probably, through an intervening neurone which may establish a connection between the sensory posterior horn and the motor anterior horn of the spinal cord. The level of the central reflex arc may be determined for many of the simpler reflexes; in the case of the patellar reflex it lies at the level of the 2nd and 3rd lumbar segments, while for the ankle-jerk it involves the 1st and 2nd sacral segments. Any injury to the spinal cord below this level leaves the reflexes unaffected while a lesion in a higher segment (transverse myelitis or degeneration of the pyramidal tract), e.g., in the dorsal or cervical cord, accentuates the tendon reflexes below. One must, therefore, assume that there arise in certain of the higher centers of the central nervous system, certain influences which act to inhibit or to regulate the spinal reflex apparatus and which are chiefly carried in the pyramidal tract. As a matter of fact the patellar reflex may be inhibited by the individual if he focus the attention upon it and at the same time voluntarily contract the quadriceps musculature. When this central inhibiting influence is removed the reflexes below are abnormally accentuated.

The transfer of the stimulus from the sensory nerves to the motor nuclei, in many reflexes, e.g., those from the skin, does not occur exclusively at a circumscribed level in the

cord; the sensory fibers passing upward in the cord send off many collateral branches to the motor nuclei in various segments. Certain cutaneous reflexes are transferred at a level above the cord in the medulla or basal ganglia and these reflexes (e.g., abdominals) are obliterated only by a lesion high up in the cord or upon interruption or degeneration of the pyramidal tracts themselves.

It is the rule with all reflexes that they are obliterated whenever the reflex arc is interrupted at any point. If, for example, the sciatic nerve be severed, neither the ankle-jerk nor the plantar reflex can be elicited. In cases of polyneuritis, e.g., following diphtheria or the abuse of alcohol, it is significant that neither the patellar, ankle nor plantar reflexes are obtainable, while in tabes, on the other hand, the tendon reflexes are lost but the plantar reflex (as a cutaneous reflex) is present and active. Reflexes are also lost if the arc be interrupted in the gray substance of the spinal cord or in the brain. With any lesion in the sacral portion of the cord the ankle-jerk is lost while the knee-jerk remains; with disease at the level of the 2nd and 3rd lumbar segments the patellar reflex cannot be elicited whereas the Achilles reflex is still present. A pathological **accentuation of reflexes** (hyper-reflexia) occurs with any transverse section of the cord above the level of the reflex arc involved, or when the inhibitory fibers, which pass downward from the brain through the pyramidal tracts to act upon the reflex centers, are degenerated and functionless. Such accentuation is evidenced by the fact that the tendon reflexes may be elicited with a very light stroke of the hammer, and, when so elicited, are abnormally extensive; further they may be obtained by striking not only the tendon but the bony region round about, e.g., the upper portion of the tibia. The increase in the extent of the reflexes is further characterized by the contraction of the muscle or muscle groups to which the tendon belongs and other adjacent groups, as well as, sometimes, those on the other side of the body. Finally, with such pathological hyper-reflexia it sometimes occurs that a single tap elicits not a single twitch but often a series of twitches. If, under these conditions, the patella be grasped between the fingers, shoved downward and held in this

position, there ensues a rhythmic series of contractions of the quadriceps (**patellar clonus**); or if the Achilles tendon be held under tension by pushing upward upon the ball of the foot (with the knee slightly bent) there follows rhythmic plantar flexion of the foot (**ankle clonus**).

The **cutaneous reflexes** represent, under pathological conditions, a very complicated series of events, since their reflex arcs are by no means limited to any definite level of the spinal cord, but also involve higher centers. Complete section of the cord in the cervical or thoracic regions, e.g., from gun-shot wound or from the pressure of a tumor, tends to accentuate the cutaneous reflexes in the lower extremities. Stroking the sole of the foot with a cold or pointed instrument leads to shortening or withdrawal of the entire extremity with dorso-flexion of the foot and flexion of the knee and hip. In this fashion the sole of the foot is withdrawn from the stimulus though the sensory impulse never reaches consciousness. In severe cases the reflex response may spread to the other leg causing it to be **extended.** Occasionally there occur alternate flexion and extension of both legs in a tramping fashion. Such a "mass reflex" may lead to involuntary evacuation of the bladder or rectum and to profuse sweating. While it is characteristic of the normal plantar reflex that the toes are bent plantarward like claws, if the cord is sectioned in the thoracic or cervical regions this reaction is altered in that the toes are spread like a fan and the great toe is slowly extended upward. This **Babinski** sign is positive whenever the pyramidal tracts are degenerated, e.g., as a result of a localized lesion in the internal capsule or in some cases of combined lateral sclerosis. Since, in children during the first few weeks of life, the Babinski sign is positive and since during this period the pyramidal tracts are known to be incompletely developed, it is to be assumed that the normal plantar reflex of the adult involves a higher reflex arc, whose ascending branch runs in the pyramidal tract, and that upon interruption of this tract the more elementary reflex reappears. With destruction and degeneration of the pyramidal tract, e.g., following a hæmorrhage into the internal capsule, the abdominal and cremasteric reflexes disappear while the knee-jerks and ankle-jerks are accentuated.

The same holds true for all forms of degeneration involving the pyramidal tracts in the lateral columns and for multiple sclerosis. One may, therefore, assume that these cutaneous reflexes as well involve a long reflex arc.

If the pyramidal tracts are suddenly interrupted, e.g., in apoplexy, or if a complete transverse section of the spinal cord occur, during the first few days to 3 weeks the cutaneous and tendon reflexes are not increased but lost, and the musculature is flaccid and hypotonic. The functions of the spinal cord seem, in such an instance, to have sustained a certain shock and to recover their activity only gradually; later there develop spasticity of the musculature and abnormal accentuation of the reflexes.

Among the clinically important reflexes are those from the **tendons, skin** and **mucous membranes** whose reflex arcs lie in the brain and cord, and **visceral** reflexes which are mediated chiefly through the nerve fibers and ganglia of the autonomic and sympathetic nervous systems.

In the semicircular canals of the labyrinth any change in position of the body, in so far as it affects the position of the head, gives rise to a sensory impulse which is transmitted, along the vestibular nerve, to the medulla. From the vestibular nucleus in the medulla tracts pass upward to the cerebellum and downward to the cord making possible the maintenance of tone of the general body musculature necessary to the preservation of equilibrium. Every movement of the head, in the presence of an intact vestibular apparatus, is associated with compensatory changes in position of the trunk and extremities. These processes are grouped together under the term suggested by Magnus, "postural reflexes." With any impairment of this complicated postural apparatus, i.e., in the semicircular canals, vestibular nerves, or cerebellum, there appear disturbances of equilibrium and posture accompanied by dizziness; the tonus of the skeletal musculature is reduced upon the affected side and the gait becomes unsteady.

Reflex phenomena may be represented as conductors, in which the various afferent sensory paths and the efferent motor paths are connected at different levels in the cord and the brain by innumerable twigs, from the simplest of

the visceral reflexes in the cord up to the most highly developed and complicated reflex phenomena in the brain. Any and all combinations of these reflexes are possible, and Sherrington speaks therefore of the **integration of reflexes**.

Pawlow designated as **conditioned reflexes** those which occurred only under certain circumstances. Thus, for example, the smell of food or the suggestion of the same brings about a secretion of saliva and of gastric juice, but only in a hungry individual, while the same suggestion immediately following a meal brings about no secretion or may even be unpleasant. Conditioned reflexes play an important rôle in the sexual function.

The most important **tendon reflexes** are:

The **patellar reflex** (knee-jerk) elicited by striking the patellar tendon (under tension) with a rubber hammer. Such a stimulus is followed by contraction of the quadriceps and extension of the lower leg. The knee-jerk may be tested with the patient sitting with one knee crossed over the other and the lower leg relaxed, or, with the patient in bed, by lifting the knee slightly, with the hand in the popliteal space. During this procedure care must be taken that the quadriceps is entirely relaxed. In certain cases the knee-jerk is obtained only upon reinforcement, i.e., directing the patient to clasp the hands and to squeeze at the time of the test (Jendrassik). Absence of the knee-jerk is known as Westphal's sign.

Achilles tendon reflex (ankle-jerk): Upon striking the Achilles tendon there results a contraction of the muscle of the calf. This reflex is best elicited with the patient kneeling on a chair.

Reflexes of the upper extremities: Striking the triceps tendon causes extension of the elbow; a blow upon the biceps tendon causes flexion of the elbow.

Closely related to the tendon reflexes are those from the **bones** and **periosteum:** A blow upon the distal end of the **radius** causes flexion of the elbow. A light tap in the region of the cuboid bone on the dorsum of the foot causes, in healthy individuals, dorsiflexion of the 2nd to the 5th toes, whereas with organic disease of the pyramidal tracts the

toes are plantar-flexed and spread (Mendel-Bechtereff). If the middle finger be pressed backward into the palm of the hand the thumb is adducted (hand reflex of Meyer). In normal individuals the knee-jerks are constantly present but the periosteo-radial and triceps are not always so.

The **cutaneous reflexes** include:

Abdominal reflexes: Stroking the skin over the abdomen with a pointed instrument causes contraction of the abdominal musculature on the same side. These reflexes are divided into upper and lower. The abdominal reflexes are sometimes absent in healthy individuals, particularly in the presence of abdominal distension.

Cremasteric reflexes: Stimulation of the inner surface of the thigh causes elevation of the testis on the same side. The cremasteric reflex is comparable to the abdominal reflex; both are absent in hæmiplegia on the side of the paralysis, and bilaterally absent in multiple sclerosis.

The **plantar reflex:** Upon stimulation of the sole of the foot by stroking, cold, or electric current, plantar flexion of the toes normally results. With vigorous and continued stimulation the leg is drawn up against the body and flexed at the hip and knee. With interruption or degeneration of the pyramidal tracts the great toe is slowly dorsiflexed upon stimulation (**Babinski's sign**).

Among the important **reflexes from mucous membranes** are the following:

Conjunctival and corneal reflexes: Closure of the eyelid upon touching the conjunctivæ and cornea; the conjunctival reflex is sometimes absent in the normal. Absence of the corneal reflex is an important sign of injury of the 1st branch of the trigeminus, e.g., with tumors at the base of the brain in the cerebello-pontine angle; it is also lost during facial paralysis.

The **pharyngeal reflex** or **gag reflex** appears upon touching the soft palate or pharyngeal mucous membrane, and involves contraction of the pharyngeal musculature. Since this reflex is irregular in normals and is prone to be absent in nervous individuals its failure is significant only when unilateral, (a sign of vagus or glosso-pharyngeal disease upon the same side).

Cough reflex, elicited upon stimulation of the larynx and trachea by foreign bodies, pus or inflammation, is absent with disease of the vagus or medulla.

Anal reflex: Introduction of the finger into the rectum brings about a vigorous contraction of the anal sphincter. With lesion of the sacral portion of the cord this reflex is lost and the external sphincter is relaxed.

Among those reflex phenomena involving sympathetic and autonomic nerves the most important are the **pupillary reflex,** and those involved in the **evacuation of urine** or **fæces,** and in the **sexual function.**

The pupils are innervated from the oculo-motor nerve, which carries fibers to the M. sphincter pupillæ, and from the sympathetic: From the medulla oblongata fibers pass to the cervical region, leave the cord at the level of the 1st thoracic segment and pass over into the cervical ganglia and paravertebral chain of the sympathetic. They then course upward with the cervical sympathetic into the cranium, and to the eye. Stimulation of these sympathetic fibers causes dilatation of the pupil (mydryasis), their paralysis constriction thereof (myosis). Stimulation of the **oculo-motor,** on the other hand, brings about constriction of the pupil; paralysis, absence of the light reflex and paralysis of accommodation. In tabes, paresis and other forms of central nervous system syphilis, the pupils are fixed to light, (fail to contract when a beam of light is thrown into the eye), while pupillary constriction still takes place during accommodation (**Argyll Robertson pupil**).

Evacuation of Urine and Fæces

The smooth muscle of the bladder wall (M. detrusor urinæ) and the internal vesical sphincter receive no direct motor nerve supply and are accordingly not under voluntary control; in common with all other smooth muscles they are supplied by sympathetic nerves. The striated musculature, on the other hand, which controls the posterior portion of the urethra (ischio- and bulbo-cavernosus, compressor urethræ) is supplied by medullated spinal nerves; hence the urine which remains in the posterior urethra after micturition may be voluntarily expelled. These striated muscles also play a

part in the voluntary interruption of micturition and in some cases of urinary obstruction. The centers for bladder function lie in the sympathetic ganglia. To these fibers pass from the spinal cord (rami communicantes) in part with the lumbar roots but chiefly from the sacral segments. These nerve tracts pass downward from the brain through the entire cord to the conus terminalis and from this through the cauda equina. If these paths be interrupted, e.g., by compression of the cauda equina or by transverse section of any portion of the cord (from myelitis or compression), evacuation of the bladder cannot be voluntarily begun; with any interruption of the sensory paths of the spinal cord the sensation of pressure beneath the symphysis, which, in the normal individual, indicates a full bladder, is lost. There results complete urinary retention, and the bladder dilates to a maximum. Complete retention may often demand catheterization, but usually lasts for only a short time. Soon small quantities of urine are involuntarily voided from time to time although the bladder still remains overfilled; it is as though the full bladder periodically overflows (**ischuria paradoxa**). After these tracts in the cord or cauda have been interrupted for some time the evacuation of urine gradually becomes automatic; every 10 to 30 minutes small amounts of urine are passed involuntarily, often without the patient having any sensation thereof and usually without complete emptying of the bladder. Persistent dribbling of urine does not occur with disease of the cord or cauda. With **tabes** and **multiple sclerosis** the patient is unable to begin micturition or, in some cases, voids involuntarily. With **disease of the brain** dysuria occurs if there are bilateral lesions of the paracentral lobules, e.g., with gun-shot wounds. **Delirious** patients sometimes void involuntarily in bed; in **coma,** on the other hand, the stimulus of the full bladder is no longer perceived and the bladder fills to a maximum.

Similar to the function of the bladder is that of evacuation of the bowels. Filling of the ampulla recti causes sensation of pressure; the contraction of the smooth musculature of the rectum, innervated by sympathetic nerves, produces tenesmus, which may be suppressed by the voluntary contraction of the striated musculature of the external sphincter.

In the act of defæcation tension of the abdominal muscles induces the peristaltic contraction of the ampulla recti. With any interruption of the spinal tracts defæcation may no longer be voluntarily controlled; it occurs involuntarily and usually at long intervals. With anæsthesia of the rectal mucous membrane defæcation may proceed without any sensation on the part of the patient. With a lesion of the sacral cord the anal reflex is lost as well as the tone of the external sphincter and the anal ring therefore remains relaxed and open.

The **sexual reflexes** in both men and women are controlled by the sympathetic nervous system, but are particularly influenced by psychic stimuli and by the degree of filling of the sexual glands.

Disturbances in potency on the part of the male may be due to deficient production of sperm or to imperfect erection. The latter condition occurs with many forms of spinal cord disease, e.g., tabes or myelitis, or due to psychic inhibition, or general debility.

MOTILITY

Any interruption or degeneration of the pyramidal tract, be it in the brain or in the cord, leads to paralysis; a single muscle group, extremity, or under certain conditions, an entire half of the body is thus isolated from the control of the motor cortex. With any lesion in the brain the **opposite** half of the body is affected (**hemiplegia**).

With a transverse section in the spinal cord **both** halves of the body are paralyzed below the level of the lesion (**paraplegia**). One speaks also of paraplegia whenever any portions of the body, e.g., the ocular muscles of both eyes, are symmetrically paralyzed. Paralysis of one extremity, one hand or one foot, is known as **monoplegia,** and occurs only with a circumscribed cortical lesion in the area corresponding to the paralyzed member.

The **peripheral motor** nerves, which pass out from the anterior horn of the cord through the anterior roots, represent the axis cylinders of large motor ganglion cells, which are grouped in the anterior horn of the cord. Disease of these ganglion cells, e.g., myelitic softening or degeneration, leads to the degeneration of the peripheral nerve fibers down to

their end plates, which lie in contact with the striated muscle fibers. With section or crushing of a peripheral nerve degeneration of the peripheral segment follows; the axis cylinder and its myelin sheath disintegrate into small fatty masses.

If a (lower) **motor peripheral neurone** be destroyed, the muscle which it supplies is completely paralyzed and flaccid; such a muscle shows the electrical **reactions of degeneration** and soon **atrophies.** The cutaneous and tendon reflexes are also lost due to the destruction of the motor limb of the reflex arc. If, on the other hand, the **central** (**upper**) **motor neurone** (pyramidal tract) be destroyed, be it due to a local lesion in the internal capsule, to section of the cord or to a gradually progressing primary degeneration of the lateral column, the motor ganglion cells of the anterior horn, and their motor nerves, remain intact and can still exercise their influence upon the muscles. The **muscles,** therefore, **do not degenerate;** both nerves and muscles retain their electrical irritability. The tendon reflexes, as well as certain of those from the skin, are not lost, but, on the contrary, are abnormally accentuated. The muscles are indeed paralyzed, i.e., they cannot be voluntarily brought into motion, but their tonus is increased. They pass into a lasting, spastic, state of contraction, which in the arm, affects particularly the flexors, but in the leg, particularly the extensors. **Clonus** and the **Babinski** reaction soon make their appearance. This **spasticity** of the muscles and **accentuation of the tendon reflexes** find their explanation in the fact that, with degeneration of the pyramidal tracts, the ganglion cells of the anterior horn have been removed from the inhibiting and regulating function of the cerebral centers, while they remain in a state of continued excitation as a result of the afferent sensory impulses.

Disease of the **central** motor neurones, that is the pyramidal tract, and that of the **peripheral** motor neurone produce, therefore, quite different clinical pictures, which are easily distinguishable. It should, however, be pointed out that certain diseases, e.g., amyotrophic lateral sclerosis, affect both systems.

In addition to the voluntary purposeful movements, innervated from the cerebral cortex via the pyramidal tract, there are various primitive muscular movements which are not under conscious control. To this group belong particu-

larly those movements and muscular contractions in the trunk which are necessary to the maintenance of an upright position, including the gross maintenance of the position of the limbs associated with almost every change in posture. These primitive movements, as well as the complicated act of sucking, are, however, to be observed in infants before either the cerebral cortex or the pyramidal tracts are fully developed. They are possibly controlled from certain primitive, and philogenetically old, motor centers in the mid and hind brain, particularly from the globus pallidus of the lenticular nucleus. These portions of the brain are abundantly medullated at birth and receive impulses from the sensory nuclei of the optic thalamus in which the centripetal impulses from the entire body are united, with the exception of those from the eyes, ears, and organs of taste.

The primitive motor centers, i.e., the globus pallidus of the lenticular nucleus, the corpus subthalamicum (Luys), the substantia nigra of the cerebral peduncles, and the red nucleus, which are also linked with the medulla, transmit motor impulses to the cranial nerves and to the cord through efferent paths which, it may be assumed, lie in part in the so-called bundle of Monakow just ventral to the lateral pyramidal tracts and are, in part, distributed throughout the lateral columns. These motor centers and their efferent tracts are grouped under the term **extrapyramidal motor system.** From them are innervated all movements which are not consciously controlled, i.e., all automatic reflex actions, e.g., reactions of defense. Through them, too, are controlled the tonus and position of the limbs and muscles upon which is superimposed the conscious control of purposeful movement via the pyramidal tracts. Disease processes in these centers, e.g., **Parkinson's disease** and certain residua or sequelæ of **encephalitis lethargica** are characterized by immobility which, affecting the musculature of expression, produces the mask-like facies; the gait is shuffling because the musculature of the trunk and of the arms no longer coordinate; all movements are so slowed by increased muscular rigidity that any rapid movement is rendered impossible. Diseases of the other extrapyramidal centers: the red nucleus, the putamen and the associated nucleus caudatus, produce

motor disturbances which interrupt the normal course of movements: choreic twitchings, athetosis and tremors.

MOTOR FUNCTION

The strength of the various muscles and muscle groups upon voluntary movement is first examined by directing the patient to make some particular movement, e.g., flexion or extension of the joints while the physician attempts to prevent it. Further simple and more complicated movements are tested as to whether they are coördinate (**eutaxia**) or uncertain and incoördinate (**ataxia**), or interrupted by involuntary movements or twitchings. The tonus, i.e., the normal tension of the muscle at rest is then examined. With increased tonus the muscles feel hard and tense and oppose an **elastic** resistance to passive, and particularly to rapid, movement (hypertonia). Still further increase in muscular tension may lead to contracture. The first evidence of such spasticity is an **accentuation of the tendon reflexes**. From this **spastic hypertonia** of musculature, which results from interruption of the **pyramidal** tracts, should be distinguished the increased **muscular rigidity** and stiffness of movement which is characteristic of disease of the **extrapyramidal system** and particularly of the lenticular nucleus. In this latter condition the muscles show no elastic resistance but rather a "lead-pipe rigidity"; they do not immediately return to their former position but follow passive movement slowly and remain in the new position for some time. At the same time the tendon reflexes are less accentuated and pathological reflexes (clonus, Babinski) are absent.

With decreased tonus (**hypotonia**) the muscles are limp; they are not resistant to passive movements. The joints, at the same time, show an abnormal degree of mobility. Abnormal flaccidity and extensibility of the muscles without loss of muscular strength is encountered particularly in tabes; in such patients the head may sometimes be laid between the knees. Those pareses and paralyses which are associated with hypotonia are designated as **flaccid paralyses**; they commonly go hand in hand with decrease or abolition of the tendon reflexes and are characteristic of lesions of peripheral motor neurones, i.e., the gray substance of the anterior horn

of the cord or the peripheral nerves. It is, however, to be noted that recent and severe cerebral paralyses sometimes show at the outset complete flaccidity of the affected limbs in which the reflexes are not to be elicited. The characteristic increase in muscle tonus and accentuation of the tendon reflexes make their appearance only after days or weeks.

Further examination should determine whether the muscles occupy a normal volume, i.e., whether or not they are atrophic: If a muscle group remain totally inactive for any considerable length of time, e.g., with pathological fixation of a limb, or if, on account of pain, the movement of a joint is limited, atrophy results; the muscle bundles become thinner and many of them may disappear. Such **atrophy of inactivity** develops sometimes following a cerebral lesion. The electrical irritability of atrophic muscles is retained but is distinctly decreased. If the motor nerve be severed or poisoned (alcohol, lead, arsenic, diphtheria toxin), its peripheral segment degenerates within a few days and is, therefore, unexcitable by an electrical current. The same results follow destruction of the large motor ganglion cells in the anterior horn or the motor nuclei of the cranial nerves. With any such destruction of the motor nerves and their end plates the striated muscles in the domain of the nerve involved are removed from nervous control; they can receive no more impulses, become entirely flaccid, and atrophy far more rapidly and completely than if they are simply inactive but retain a normal nerve supply. Obviously if the nerve be destroyed the muscle can no longer be excited by electrical stimulation of its nerve. A rapidly interrupted faradic current acts exclusively through the nerve and its end plates; in the presence of peripheral nerve degeneration, therefore, the muscle no longer responds to faradic current. A **denervated muscle** still reacts to the make and break of a galvanic current, not with the quick twitch characteristic of the normal muscle, but with a slow lazy contraction. This **reaction of degeneration** is present in all those conditions in which either the anterior horn of the cord, the nuclei of the motor cranial nerves or the motor spinal nerves themselves have undergone injury.

In the case of degeneration of the motor ganglion cells in the anterior horn or of the motor nuclei of the cranial nerves,

e.g., with spinal muscular atrophy or bulbar paralysis, there occur **fibrillary twitchings** in the degenerating muscles, i.e., irregular contractions of isolated muscle fibers or groups of fibers. These fibrillary twitchings fail to appear, however, unless the peripheral nerves are intact. In peripheral nerve palsies the muscles are always flaccid.

In a similar fashion it is possible to differentiate between central and peripheral paralyses affecting the **motor cranial nerves**. Cerebral disease never leads to paralysis of a single ocular muscle and hence never causes diplopia or impairment of motion of one eye alone; in such cases **both eyes deviate** to right or to left. This **conjugate deviation** appears with localized lesions in the region of the gyrus angularis or occasionally with lesions in the frontal lobe. In contrast with this, disease processes involving the **nuclei** of the **nerves** supplying the **ocular muscles**, lying beneath the corpora quadrigemina and in the region of the pons, lead to paralyses of **single ocular muscles** and hence to inability to fix both eyes upon the same point; **diplopia** is the inevitable result. Such is the case with lesions of the motor nerves to ocular muscles, i.e., the oculomotor, trochlearis and abducens. These nerves are not infrequently involved at some point along their course in cases of basilar meningitis.

With **central paralysis** of the **N. facialis**, i.e., with destruction of the path from the cerebral cortex through the internal capsule to the nucleus facialis on the **opposite side**, the paralysis tends to involve chiefly the middle and inferior branches, i.e., the muscles of the cheek and lips, while the musculature of the forehead and the obicularis palpebrarum remains unaffected or only slightly so. The electrical excitability of the facialis remains intact; contracture of the paralyzed half of the face sometimes follows after a considerable period. With **peripheral facialis paralysis**, involving the facial nucleus in the medulla or the nerve at some point along its course, the paralyzed muscles on the **same side** are flaccid and paralysis involves the entire domain of the facial nerve including the muscles of the forehead and the obicularis palpebrarum.

With central paralysis of the **hypoglossus** the tongue deviates to the opposite side when thrust out, the musculature of the paralyzed side of the tongue is not atrophic and the

mobility of the tongue remains almost unimpaired. With lesions of the **nucleus** hypoglossus or of the nerve along its course, **the same side** of the tongue is transformed into a flaccid sac. In cases in which the nucleus is involved, e.g., with bulbar paralysis, the tongue shows active fibrillary twitchings and the characteristic reaction of degeneration.

Ataxia

Ataxia is a condition in which, while the muscles may retain their normal strength, they are unable to accomplish coördinate action; movements previously performed with dexterity are now accompanied by considerable wavering. One tests for ataxia by directing the patient to carry out certain complicated movements: to touch the nose with the tip of the finger, to write, to walk a straight line, or to touch the patella of one leg with the opposite heel. Ataxia in the legs makes itself apparent by the fact that the patient stands upon a wide base, and tends to stagger upon walking. Ataxia is due to loss of deep sensibility; this disturbance of sensations in the muscles, tendons and joints removes their movements from the constant control of the muscle sense (**sensory ataxia**). This is principally the case in **tabes dorsalis**. The ataxia commonly observed with peripheral neuritis, due either to alcohol or diphtheria toxin, is to be explained in the same fashion. When the patient is not able to control his movements with the eyes (in the dark or with the eyes closed) this form of ataxia is considerably accentuated. If such a patient attempt to stand with the feet together and the eyes closed he sways and may fall (**Romberg's** phenomenon).

Ataxia is also observed with disease of the **motor cortex** (cortical ataxia), and with disease of the cerebellum. This **cerebellar ataxia** manifests itself chiefly in uncertainty of position and in swaying on any attempt to walk or stand (**static ataxia**). It is not affected by control with the eyes, and is not increased, therefore, when the eyes are closed. That form of ataxia which occurs with multiple sclerosis and which is manifest not so much by uncertainty of movements as by intention tremor, is perhaps to be explained upon the basis of disturbances of the coördinating centers; it is not usually affected by closure of the eyes.

MOTOR SYMPTOMS

Spasms are gross, involuntary muscular contractions. Two types are distinguished:

Clonic spasms consisting in repeated quick twitchings and **tonic**, tetanic muscular contractions.

Clonic spasms involving the whole body are known as **convulsions**; if the tonic rigidity involve the entire body musculature or a large proportion thereof one speaks of **tetanus**. Trismus consists in the tonic spasm of the musculature of the jaw.

Convulsions may occur with various diseases of the brain and particularly those in which the cortex is stimulated or injured, i.e., with tumors in or near the cerebral cortex, or with any condition which brings about an increase in the intracranial pressure, e.g., meningitis. With diseases which involve the motor portion of the cortex the clonic convulsions usually begin in that muscle group corresponding to the diseased or stimulated cortical area, i.e., in the musculature of the left side of the face if the focus be in the lower portion of the right anterior central fissure, and then spread corresponding to the distribution of the motor cortical centers; in the case in point to the left arm and then to the left leg. Loss of consciousness usually occurs only when the convulsions have begun to involve the other side of the body. Such convulsions, due to a cortical lesion and progressing in a regular fashion, are known as **Jacksonian epilepsy**.

In **genuine epilepsy** the attack begins, sometimes after some premonitory sensory impression (aura), with a sharp cry and generalized tonic spasm, which usually involves the muscles of respiration and leads therefore to cessation of respiration and to cyanosis. The patient falls, and there follow almost at once clonic convulsions, during which the patient may bite the tongue or otherwise injure himself. After the cessation of the convulsions the patient remains for a time in the unconscious condition which characterizes the entire attack, and then awakes rather confused. During the attack, and sometimes for a certain period thereafter, the pupils remain fixed. The patients are almost never able to recall the attack in detail. In addition to these gross seizures (grand

mal) there occur less severe attacks in which the patient loses consciousness for not more than several seconds or minutes, and in which convulsions do not occur (petit mal).

Convulsions with unconsciousness also occur with uræmia as a result of acute or chronic nephritis, and with eclampsia. Such seizures are not infrequently observed in children and particularly in those who are abnormally excitable, in the beginning of febrile diseases, with gastro-intestinal disturbances and with spasm of the glottis (see page 21).

Tetanus, (in a narrow sense lock-jaw), is a condition characterized by spasm of the entire body which is either persistent or, more commonly, occurs in attacks following any, and often slight, stimulation, and is accompanied by trismus and opisthotonus. This disease which begins with fever and pain following an incubation period of 4–14 days, and is often fatal, is caused by infection of a wound with tetanus bacillus (see page 356).

Tetany is a chronic disease far removed from tetanus. In tetany there occur tonic spasms of the hands with flexion of the arms, and sometimes cramps in the face and lower extremities. Constriction of the upper arm of such patients brings about spasm of the hands (**Trousseau's sign**). The excitability of the nerves is so increased that a tap upon the facial nerve brings about a lightning-like contraction of the facial musculature (**Chvostek's sign**). The electrical irritability is also raised; muscular contraction follows a very weak galvanic stimulus (**Erb's sign**). The **leg phenomenon of Schlesinger** is as follows: if the hip joint be abducted with the knee joint extended there develops after 1–2 minutes an extensor spasm in the knee joint upon supination of the foot. Tetany occurs following removal of the parathyroid glands, in certain diseases of the stomach (pyloric obstruction), in pregnancy, and in **spasmophilia** of children. This condition occurs in severely rachitic children and is associated with spasm of the glottis and increased nervous excitability.

Tremors may occur during voluntary movement and particularly during movements which involve a certain precision: **Intention tremor** (e.g., in multiple sclerosis), or in resting muscle, e.g., with **paralysis agitans** (Parkinson's disease).

Parkinson's disease is characterized by rhythmic tremor and shaking of the fingers, hands and feet and sometimes, also, of the head, which is most striking in the resting muscles and less striking or absent upon motion. All movements are slowed, facial expression immobile and mask-like, posture stiff and bent forward, knees bent, gait characterized by small steps and a tendency to fall forward. Generalized muscular rigidity. The disease is incurable and leads, in the course of years, to greater and greater restriction of mobility. An almost identical disease picture results following certain cases of encephalitis lethargica.

A very rapid, fine tremor of the hands is characteristic of **hyperthyroidism**; a more gross tremor is observed in **lead poisoning** (tremor saturninus), with chronic mercurial poisoning (tremor mercurialis), in alcoholism and in old age. Gross tremor of a single extremity, or rarely of the entire body, and sometimes a genuine shaking tremor is not infrequently observed in severe functional neuroses and particularly after fright; e.g., at the front during the war, or after severe psychic shock.

Tremor of the eyeball is known as **nystagmus**; both bulbi may move about the sagittal axis (nystagmus rotatorius) or there may be only a series of twitching movements in the horizontal direction. **Nystagmus horizontalis** is most striking if the patient look to one side. This form of nystagmus occurs frequently with multiple sclerosis, and with disease of the cerebellum or vestibular apparatus. In the latter condition it is important to determine whether the nystagmoid movements are directed chiefly to the right or to the left (it is the slow phase of the eye movement which is significant in this connection and not the rapid twitch back to the normal position). Both types of nystagmus may occur congenitally, particularly in asthenopia or in albinos.

Choreic movements are involuntary and uncoördinated movements of the extremities and facial musculature which may interrupt or inhibit voluntary movements. They are most frequently observed in St. Vitus' dance (chorea minor) and are possibly related to functional disturbances in the region of the putamen, the posterior portion of the thalamus

or cerebral peduncles. They may be unilateral after certain cases of hemiplegia. In chorea the musculature is hypotonic.

In contrast with such movements is a variety which are characterized by uniformity and by the fact that they are limited to certain muscle groups; these latter are known as **tics** and appear most frequently in the muscles of the neck and shoulders or face. A typical example is the repeated act of turning the head to the side and raising the shoulder at the same time.

Athetoses are involuntary irregular contractions of various muscle groups which lead, sometimes to generalized contraction, and sometimes to slow transient movements of a single portion of a limb, i.e., the hand. They appear occasionally following hemiplegia and are then limited to the paretic half of the body. Athetoses are principally observed with diseases in the region of the cerebral peduncles, or of the red nucleus in the subthalamic region, or in the lenticular nucleus. Bilateral athetosis, without any indication of paralysis, may appear with bilateral degeneration of the above regions of the brain, and particularly of the putamen.

Associated movements are involuntary movements, e.g., of the face or arms, which accompany voluntary movements of other portions of the body, e.g., with walking. They appear in some cases of hemiplegia and particularly with infantile paralysis.

With cerebral hemiplegia Strumpell's phenomenon is often observed: If the patient attempts to bend the paretic leg at the hip and knee joint the tendon of the tibialis anterior is drawn upward and the foot is drawn inward and dorsiflexed; it is, in general, a sign that muscular movement is possible only when it involves groups which are functionally connected, whereas contraction of individual muscles is no longer possible.

Electrical Reactions

These must be tested with both **faradic** (interrupted) and **galvanic** (constant) current and by **direct** application to the muscle as well as **indirect** stimulation of the muscle through the nerve. One, the **indifferent,** pole (large flat electrode) is placed upon the sternum or back, the other,

different, pole over the nerve or muscle to be tested. The different electrode should be small in order that the current may be applied with the greatest concentration at the point to be stimulated. This concentration increases inversely with the size of the electrode and directly with the strength of the current.

The electrodes themselves and the skin of the patient should be thoroughly wet with warm water to reduce the

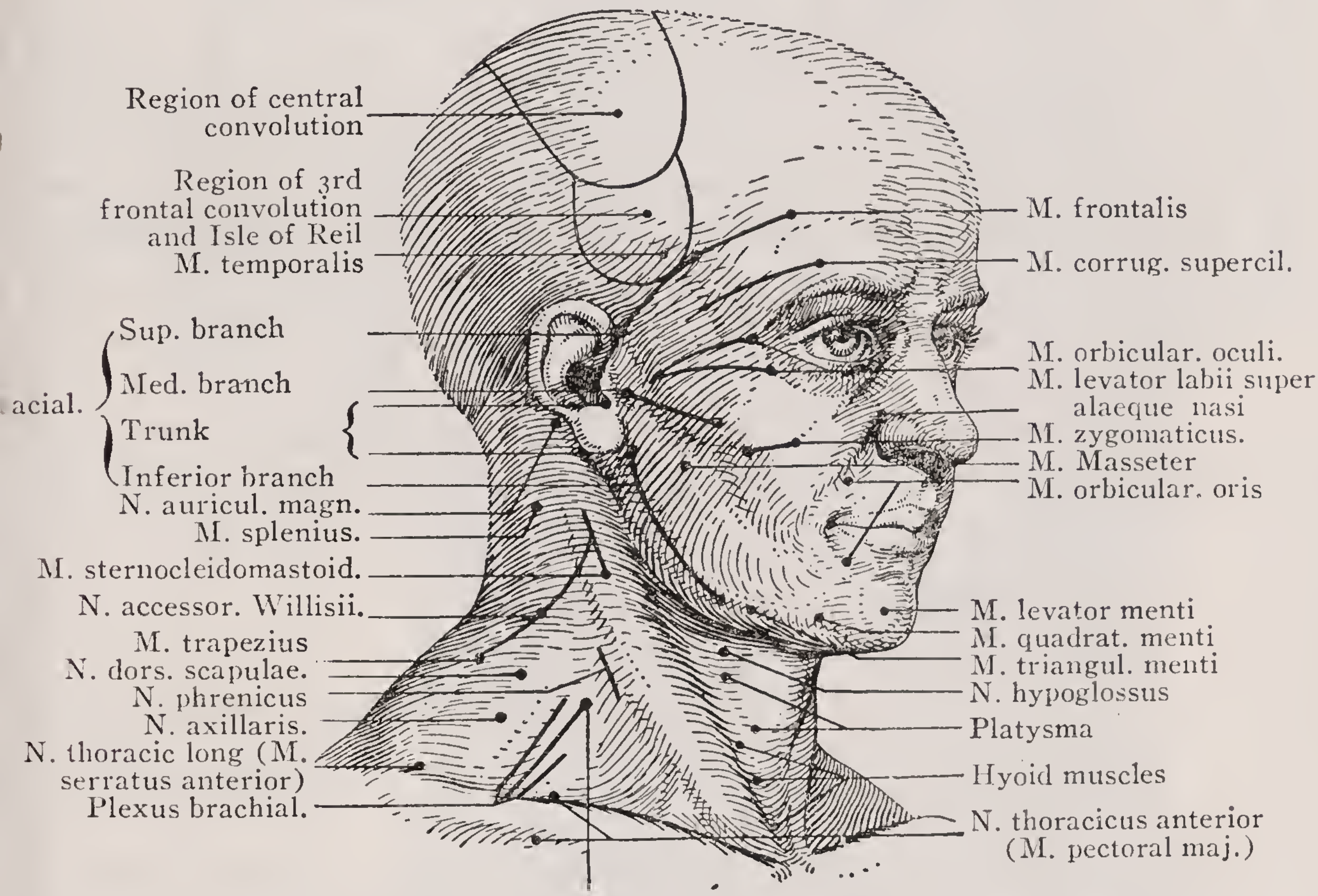


FIG. 145.—Erl's supraclavicular point (M. deltoideus, biceps, brachial, intern. brachioradialis, infraspin. und subscapular.).

resistance to the minimum. The positions of the points from which a nerve or muscle may be stimulated is indicated in figures 145–149. With increasing current strength one determines the level at which the first minimal muscular contraction appears. One begins with the **faradic** current. As a measure of the intensity of current the displacement of the secondary coil is recorded in millimeters; the current becomes stronger the nearer the secondary to the primary and strongest when the secondary is pushed completely over the primary. The faradic current may be further reduced in intensity by removing the iron core from the primary; the current is stronger

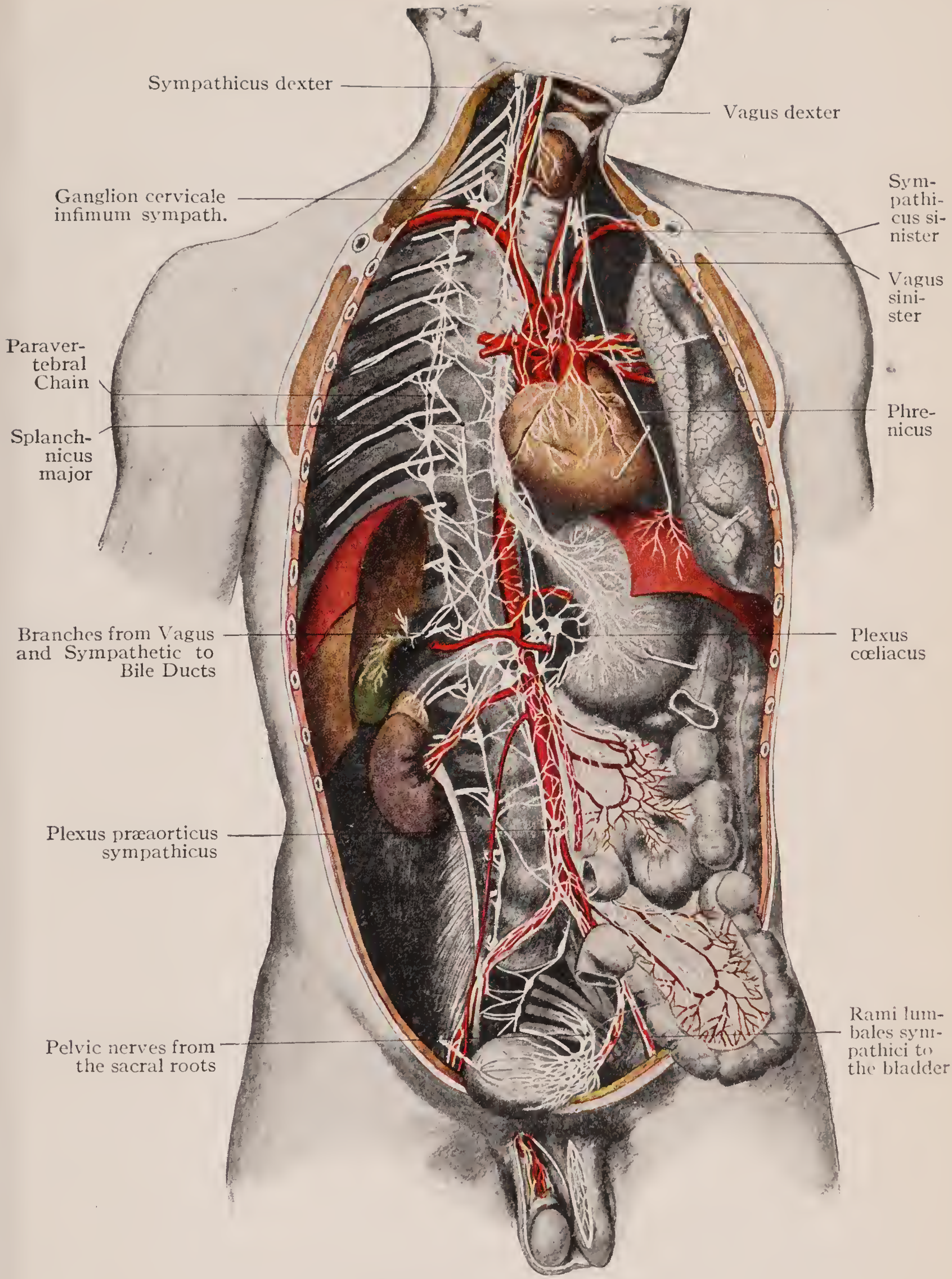
the farther the core is pushed in to the primary spool. The current is therefore strongest when both coils are pushed together and the iron core is in place. In testing with the **galvanic** current the cathode[1] (negative pole) is applied to the nerve or muscle in question. One next determines the least intensity of current which will produce a contraction in the muscle upon closing of the switch, by starting with the least intensity and gradually increasing this by throwing out the resistance in the rheostat (cathodal closure contraction, CC). The intensity of current may be measured with a galvanometer. The current is next reversed making the stimulating electrode the anode (positive pole) and the minimal current strength necessary to produce a contraction is determined upon closing (anodal closure, AC) and opening (anodal opening contraction, AOC). Both closure and opening of the current must be performed without displacement of the electrode.

Under normal circumstances stimulation takes place with increasing current strength in the following order:

Cathodal closure: CC.
Anodal opening: AO.
Anodal closure: AC.
Cathodal closure tetanus: CCT (continued contraction upon cathodal closure).
Cathodal opening: CO.

that is, using the minimal effective current strength, a contraction results only upon closing the circuit while the stimulating electrode is the cathode; with slightly stronger current the cathodal closure contraction is stronger and a twitch also appears if the stimulating electrode be made the anode, both upon opening and closure of the circuit. With still greater intensity of current closure of the circuit with the cathode as a stimulating electrode results, not in a single twitch but in a tetanic contraction of the muscle, whereas closure and

[1] To differentiate between the two poles, the ends of the wires are placed in concentrated solution of potassium iodide; there appears at the anode a blue cloud of free iodine. Or more simply the ends of the wires may be dipped in water; the cathode may be identified by the hydrogen gas bubbles which accumulate about it; the oxygen which is formed at the anode rapidly passes into solution and forms no bubbles.



The autonomic Nervous System
(Nervus sympathicus, Vagus, Pelvicus)

From the neurological charts by Müller—Hiller—Spatz
Published by J. F. Lehmann, Munich

opening still produce a single twitch at the anode. Gradual increase in the current strength beyond this point elicits a contraction at the cathode upon opening the circuit.

This rule holds principally for the indirect stimulation of the muscle through its nerve; upon direct application of the electrode to the muscle contraction is obtained principally upon closure and under these circumstances the anodal closure strength lies much closer to that of the cathode. The contractions are normally short and very rapid.

The current strength (I) is expressed in milliamperes and may be measured with a galvanometer. According to Ohm's law $I = \frac{E}{R}$, i.e., intensity of current (I) is proportional to the electro-motive force (E) and is inversely proportional to the sum of all the resistance (R) in the circuit. One ampere is that intensity of current (I) produced by the passage of an electro-motive force (E) = 1 volt through a circuit of resistance (R) = 1 ohm. One ampere is therefore proportional to $\frac{1 \text{ volt}}{1 \text{ ohm}}$; 1 volt is 9/10 the electro-motive force of a Daniell cell, 1 ohm is the resistance of a column of mercury 106 cm. in length and 1 sq. mm. in diameter. For medical purposes a current strength is employed of at most 20 milliamperes. In the case of the superficial motor nerves cathodal closure contraction occurs normally with a current strength of 1–3 milliamperes.

The intensity of current is varied either by interposing more elements or by means of a rheostat through which various amounts of resistance may be interposed. If the rheostat is connected, as is customary, in shunt, the main current which passes to the body is the greater the greater the resistance in the rheostat; if, on the other hand, the rheostat is in series, any increase in resistance diminishes the current strength.

The **resistance** of the dry epidermis is at the beginning very high (about 4000–6000 ohms); after application of the galvanic current, and particularly if the skin be thoroughly moistened, this resistance falls to about 2000 ohms so that

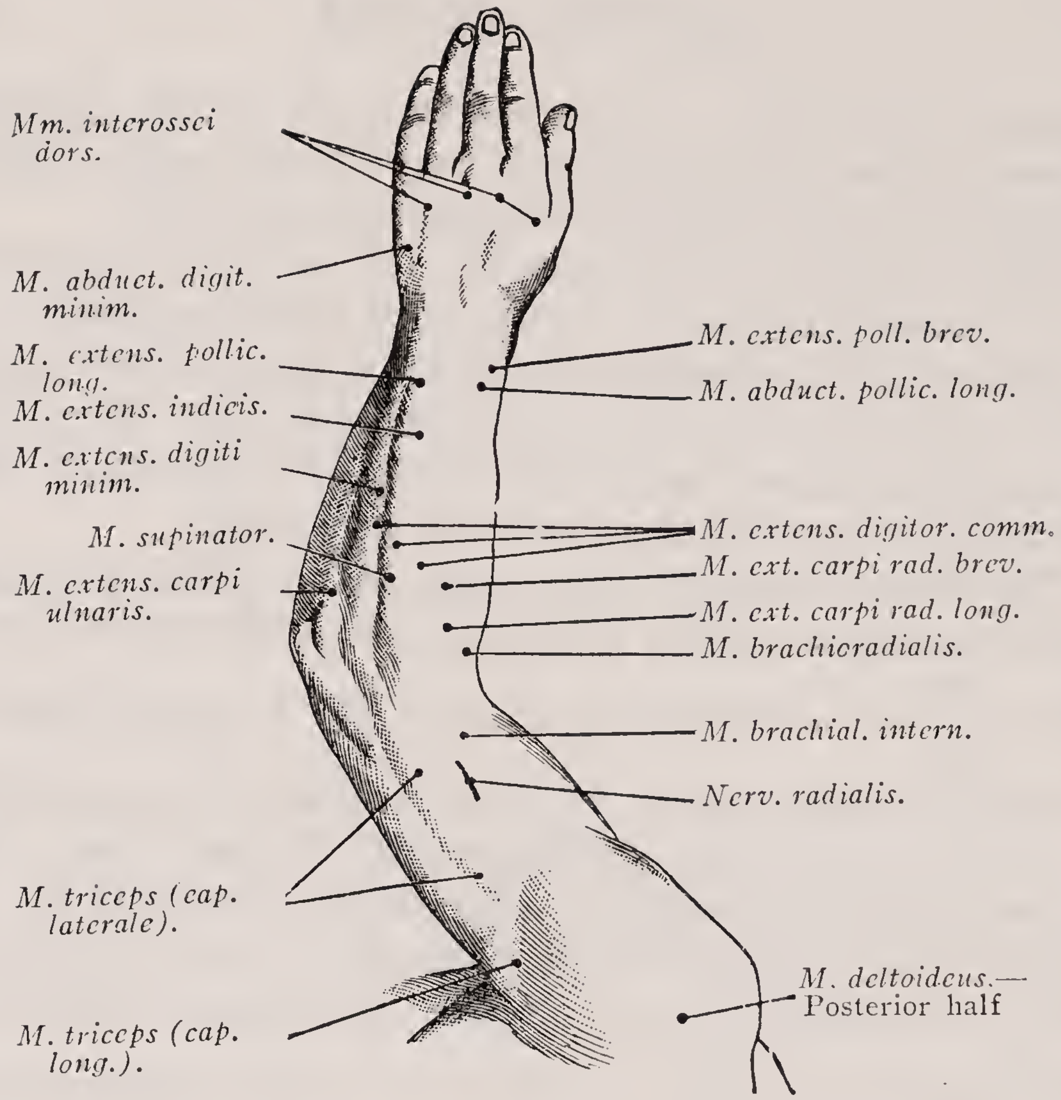


Fig. 146.

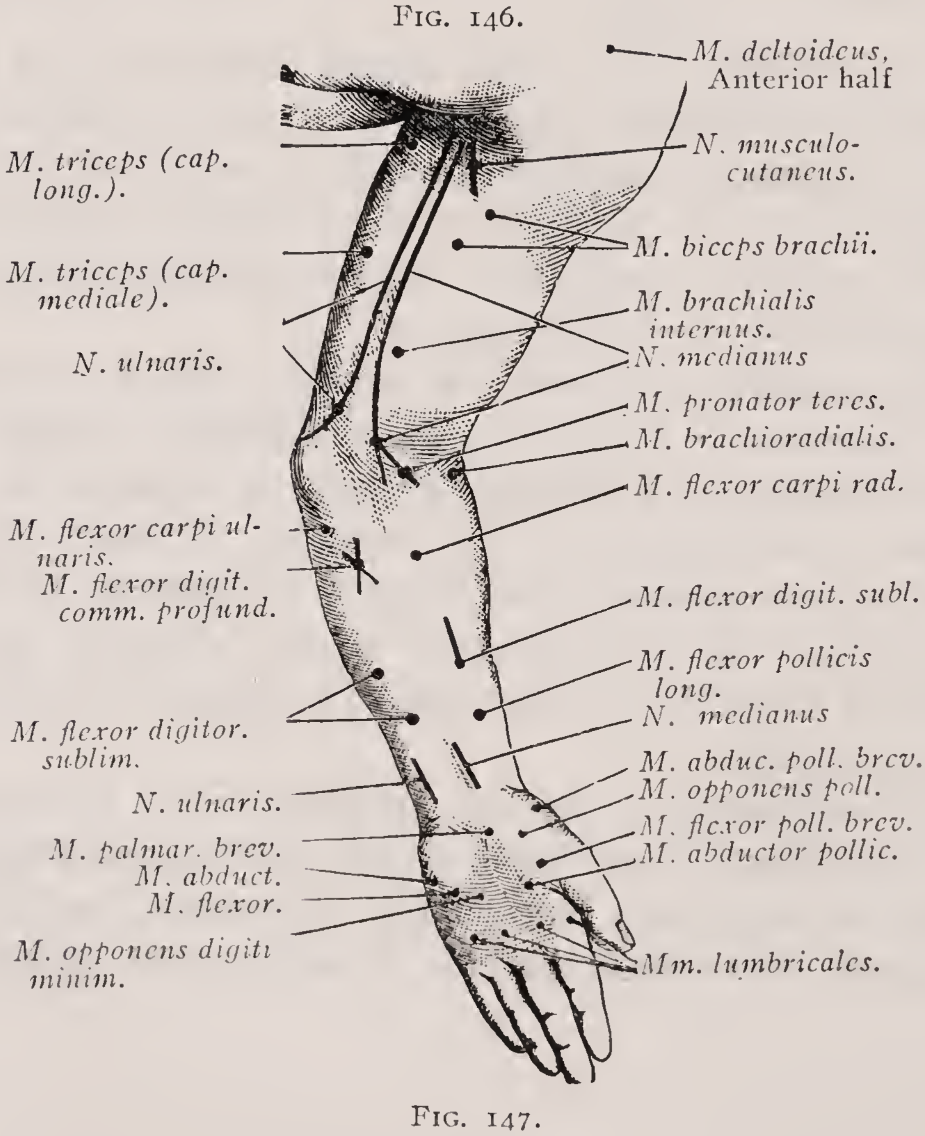


Fig. 147.

the intensity of current gradually becomes more effective if the electrodes are left in the same place. A current which, in the beginning of the examination, is of insufficient strength to stimulate may become adequate if allowed to flow for some time, due to the fall in skin resistance.

In **hyperthyroidism** the resistance of the thin skin, which

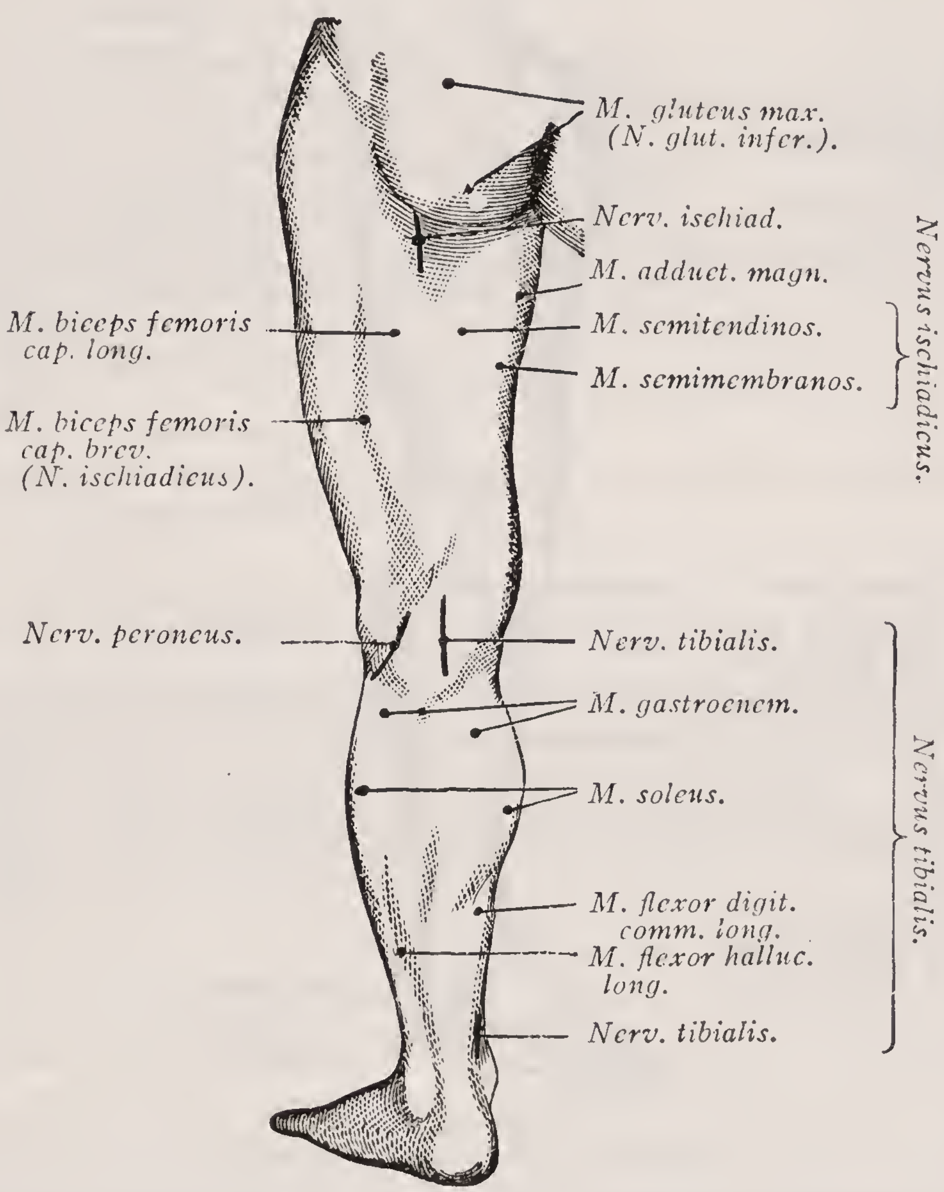


FIG. 148.

is almost always moistened with sweat, is considerably decreased while in **myxœdema** it is conspicuously high.

Quantitative changes in electrical irritability.

Simple increase or decrease may be demonstrated by a comparison of symmetrical areas on the two sides of the body: e.g., **N. frontalis, N. ulnaris** just above the olecranon, or **N. peroneus** just above the head of the fibula. At the same

time it is to be remembered that the skin resistance varies in different parts of the body and from individual to individual.

Increase in electrical irritability, to such an extent that a current strength ineffective in the normal produces definite muscle contraction, is found in tetany and after lightning

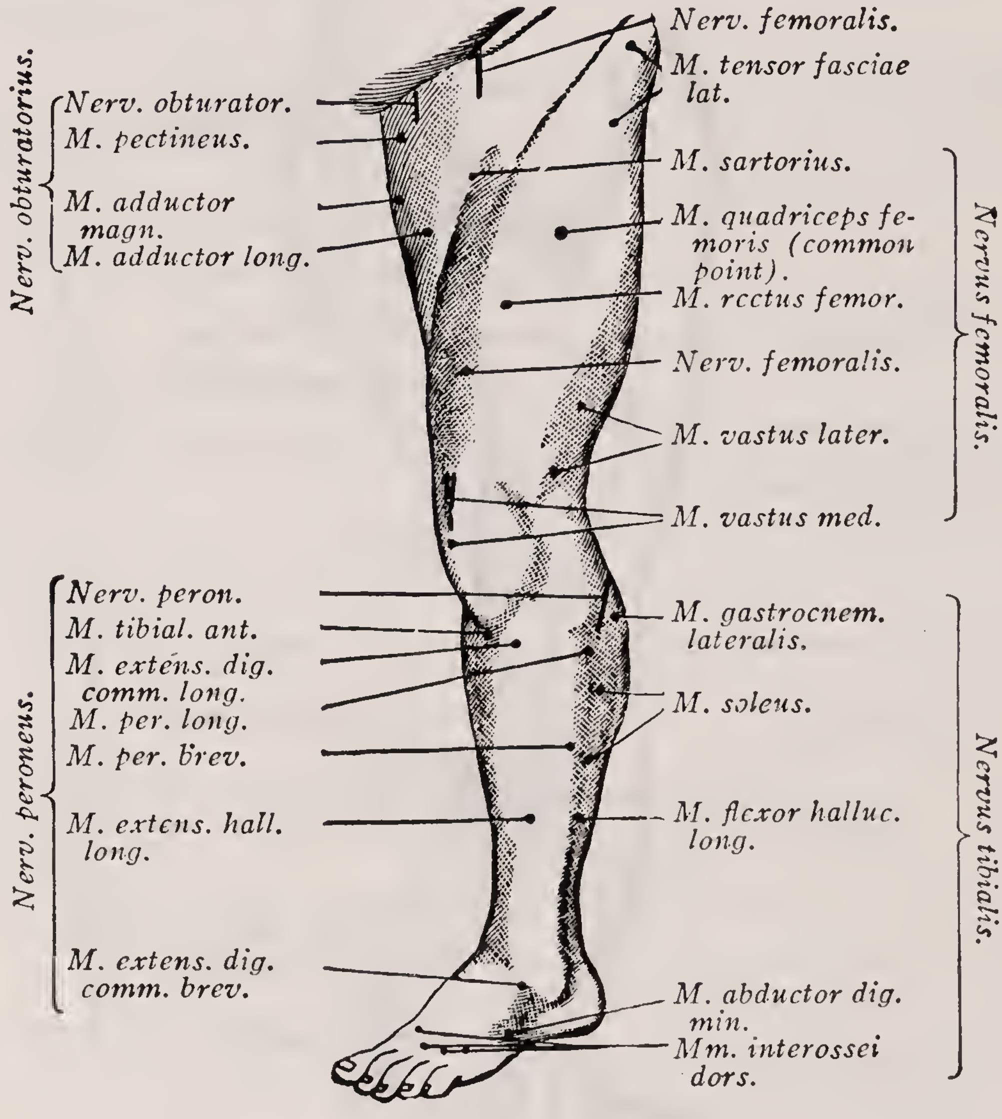


Fig. 149.

stroke. **Simple decrease** is met with in all cases of paralysis after a certain period, particularly in those forms associated with muscular atrophy, e.g., cerebral paralysis, and muscular dystrophy. In some cases the irritability is so strikingly reduced that contraction is only effected with the strongest possible current.

Using an electrode of 2 cm. diameter the electrical threshold in healthy individuals is, according to Stintzing, as follows:

Nerve	Excitability	
	Galvanic in milliamperes	Faradic in mm. coil displacement
Facialis	1.0–2.5	130–110
Musculo-cutaneous Ulnaris Medianus	0.1–1.5	140–110
Radialis	0.9–2.7	120– 90
Femoralis	0.4–1.7	120–100
Peroneus	0.2–2.0	127–100

Since different forms of faradic apparatus produce different strengths of current with the same position of the secondary coil, it is best to calibrate them upon a normal individual.

Qualitative changes in electrical irritability: **Reaction of degeneration.**

If a motor nerve undergoes degeneration its electrical irritability falls rapidly during the course of a week and, by the beginning of the second week, is entirely lost, both for faradic and galvanic current. The muscle supplied by such a nerve shows a reaction to electrical stimulation different from that of the normal muscle. The **denervated muscle** is entirely unexcitable to faradic current of short duration; it remains, however, for weeks, excitable to direct stimulation with galvanic current. However, instead of reacting, as does the normal muscle, with a quick contraction, it responds with a slow worm-like movement and this reaction is further altered in the sense that the anodal closing and opening contraction are elicited at a lower intensity of current than the cathodal closure contraction. The direct excitability for galvanic current may be extremely high in the first weeks; later it falls gradually and after a few months is entirely lost. The denervated muscle degenerates so completely in the course of months that practically no fibers remain. If, now, its nerve be reunited so that the peripheral degenerated portion may gradually regenerate, the electrical irritability seldom returns to normal before 3–4 months. This same holds

true for any injury to a nerve, e.g., by crushing or poisons. The motor nerves also degenerate following destruction of

REACTION OF DEGENERATION (AFTER ERB).

1. Complete reaction of degeneration with incurable peripheral paralysis (motility of the muscles, supplied by the nerves destroyed, is permanently lost).

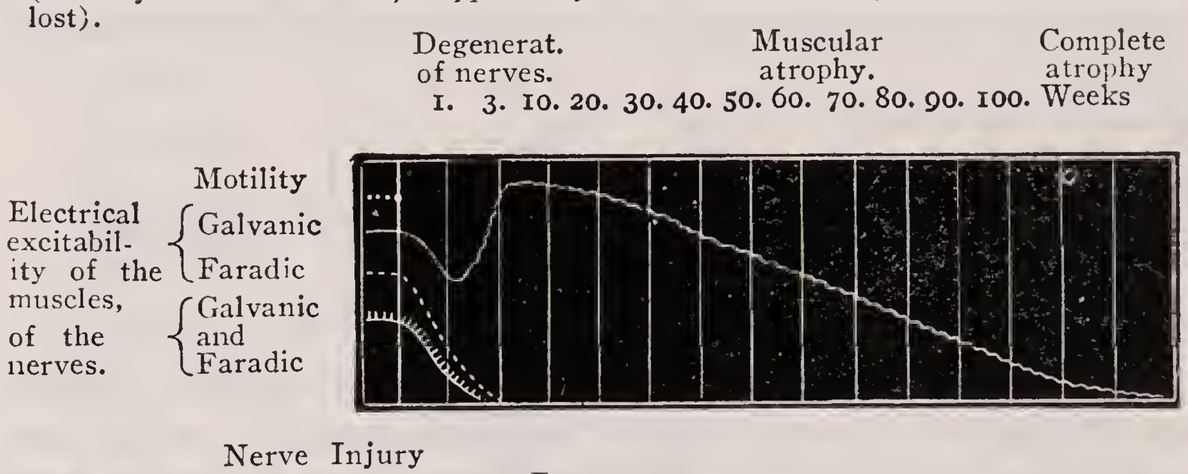


FIG. 150.

2. Complete reaction of degeneration in severe but reparable injury to peripheral nerves.

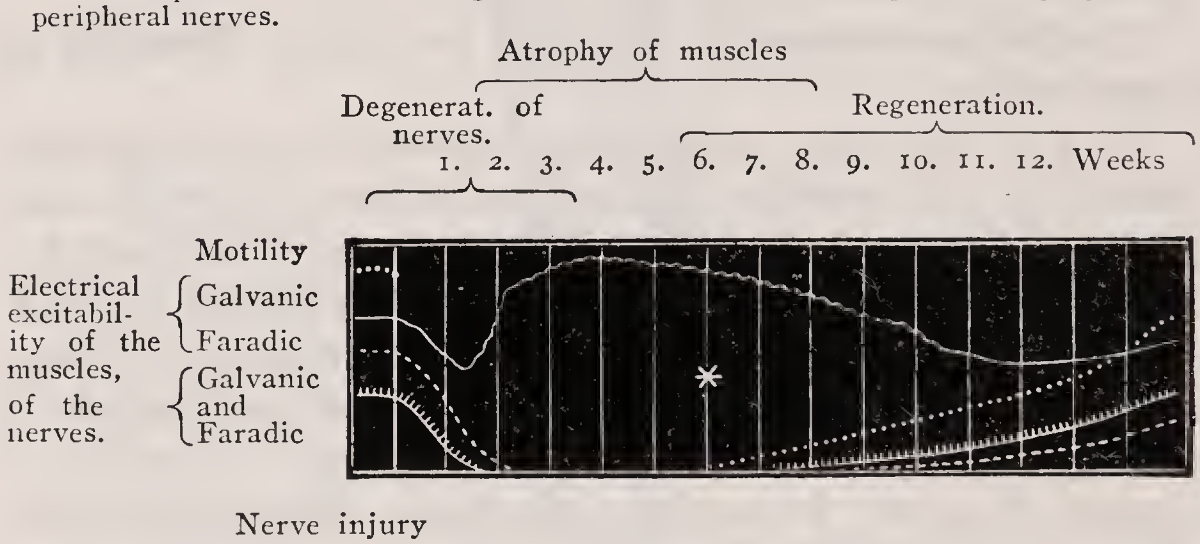


FIG. 151.

3. Partial reaction of degeneration in mild injury to nerve with rapid recovery.

FIG. 152.

their motor nuclei in the anterior horn of the cord or medulla.

This **complete reaction of degeneration** occurs only in

very severe lesions of the nerves (complete section, severe neuritic degeneration, or total destruction of the motor nuclei). With less severe injuries the reaction of degeneration is either incomplete (**partial reaction of degeneration**) or absent. The irritability of the nerve is then retained but is reduced to faradic current along with that of the muscle. With direct galvanic stimulation of the muscle the contraction is slowed and the anodal closure is greater than the cathodal closure; the former is characteristic of the reaction of degeneration.

If a complete reaction of degeneration be present it may be assumed that one is dealing with a severe paralysis from which recovery is not to be anticipated, or only after several months. If, on the other hand, in a case of peripheral paralysis, the normal electrical irritability is retained, rapid and complete recovery is reasonably to be expected. The presence of a partial reaction of degeneration indicates a prognosis somewhere between these two extremes.

The reaction of degeneration occurs with traumatic or **degenerative destruction of the peripheral motor nerves,** e.g., in lead poisoning, polyneuritis as a result of alcoholism, diphtheria or infectious diseases, and in addition with disease of the **anterior horn cells** or **motor nuclei** in the medulla, e.g., infantile paralysis, progressive muscular atrophy, bulbar paralysis, amyotrophic lateral sclerosis and myelitis.

The reaction of degeneration is absent in all cerebral paralyses, e.g., hemiplegia, and in those spinal forms whose cause lies central to the motor ganglion cells in the anterior horn or to the nuclei of the cranial nerves; in addition it is, of course, absent in all psychogenic and myopathic forms of paralysis.

In **Thomsen's disease** (see page 463), in addition to increased irritability of the muscles there occurs increase in the duration of muscular contraction upon stimulation with strong faradic current; following stimulation with strong galvanic current the relaxation takes place slowly. Upon the application of a constant current there occur rhythmic, wave-like, muscular contractions which pass from the cathode toward the anode (**myotonic reaction**). With myasthenia gravis the muscles rapidly fatigue, when stimulated by an

electric current, so that, upon repeated stimulation, the contractions gradually decrease in amplitude and finally disappear. In some cases of trichinosis the contractions in the affected muscles are considerably slowed.

SUMMARY OF SYMPTOMS AND SIGNS OF VARIOUS DISEASES OF THE NERVOUS SYSTEM

Intracranial tumors (brain tumors) produce certain constitutional symptoms: Severe headache, vomiting, sometimes convulsions, papillœdema, psychic disturbances and finally stupor. Such tumors also give rise to localizing motor or sensory symptoms or signs, e.g., anosmia (with frontal lobe tumors), hemianopsia (with occipital lesions), dizziness (with cerebellar tumors), unilateral deafness with loss of the corneal reflex (with tumors of the cerebellar pontine angle and N. Acusticus). These local symptoms facilitate the localization of the tumor and may determine the site of operative approach.

Tumors of the spinal cord lead in time to progressive damage or interruption of the motor or sensory paths in the spinal cord. Localization of such tumors depends upon the accurate determination of the segments in which the sensory, motor, or reflex disturbances have taken place. More accurate localization of a spinal cord tumor may be accomplished by means of an injection of lipiodol into the subarachnoid space following suboccipital puncture; the position of this opaque substance in the spinal canal is then determined by means of the X-ray. If the subarachnoid space is interrupted by pressure from the tumor the injected opaque substance fails to fall to the base of the spinal canal when the patient assumes the upright posture. In those conditions, in which the free circulation of the cerebro-spinal fluid in the subarachnoid space of the spinal cord is impeded, e.g., with compressing tumors or meningeal adhesions **Queckenstedt's test** is of value (page 241); the elevation of spinal-fluid pressure within the cerebral ventricles following compression of the jugular veins is no longer transmitted to the fluid in the spinal canal and thus cannot be demonstrated by lumbar puncture.

With spinal cord tumors or subarachnoid hæmorrhage the spinal fluid sometimes is colored a brownish yellow **(xanthochromia)**.

Encephalitis lethargica is an epidemic disease which tends to affect the motor nuclei of the lenticular nucleus, the subthalamic region and the substantia nigra and only seldom extends to the cortical substance. The disease begins with fever and often is characterized by somnolence. Extraocular paralyses and nystagmus and in children choreic movements often occur. As the disease progresses somnolence may give place to insomnia together with spasticity and tremors and that condition designated as post-encephalitic Parkinsonian syndrome. At this stage the disease may closely resemble paralysis agitans.

Acute anterior poliomyelitis (Heine-Medin's disease) is an epidemic infectious disease, usually beginning with fever and sometimes with sore throat, characterized by degeneration and inflammation in the gray matter of the anterior horn; it is most common in children as a spinal paralysis but occasionally appears in adults. It brings about flaccid paralysis of various muscle groups or of an entire extremity, which is greatest in extent at the outset, later diminishes, and finally remains stationary; the paralyzed muscles undergo atrophy. The tendon reflexes involving the paralyzed muscles are lost; reaction of degeneration is positive; sensibility intact, bladder and rectum rarely involved. Concerning the causative agent see page 363. If such degeneration or inflammation involve not only the gray matter of the anterior horn but the entire cross section of the cord, one speaks of **transverse myelitis.** This may be caused by the same agent as anterior poliomyelitis but is far more frequently due to other infectious agents and may result from the most various pyogenic or infectious processes. Heine-Medin's disease may attack not only the cord but also the brain, the brain stem, or the medulla, producing thereby acute and alarming symptoms of paralysis of various brain centers, or, by paralyzing respiration, may prove fatal.

So-called **chronic anterior poliomyelitis** has nothing in common either as to ætiology or pathology with acute poliomyelitis; it is closely related to, or identical with, **spinal (progressive) muscular atrophy** and is characterized by progressive and gradual destruction of the motor ganglion cells in the gray anterior horn, leading, in the course of months or

years, to advancing paralysis and atrophy. It usually begins in the small muscles of the hand and then proceeds to those of the arm and shoulder girdle; less often involvement of the motor nuclei of the medulla leads to a picture of **bulbar paralysis.** The degenerating muscles show fibrillary twitchings and the reaction of degeneration. **Amyotrophic lateral sclerosis** is distinguished from spinal muscular atrophy only by its somewhat more rapid course, and by the fact that, in addition to involvement of the anterior horn, there is degeneration of the lateral columns of the cord. There results accentuation of the tendon reflexes, particularly in the lower extremities, and a spastic gait. Amyotrophic lateral sclerosis is also frequently associated with bulbar paralysis. In all these diseases, i.e., chronic poliomyelitis, spinal muscular atrophy, and amyotrophic lateral sclerosis, sensibility, bladder function and pupillary reflexes remain quite intact.

With **progressive bulbar paralysis** there occurs gradually advancing degeneration of the motor nuclei in the medulla: Atrophy and paralysis of the lips, tongue, palate and larynx, leading to indistinct speech (anarthria), which later becomes unintelligible and toneless, dysphagia, and inadequate closure of the pharynx from the nose. On account of the insufficient approximation of the vocal cords phonation becomes impaired and bits of food cannot be prevented from passing into the respiratory passages. Here again there occurs no disturbance of sensibility, nor of function of the bladder or rectum. Bulbar paralysis may either precede or follow spinal muscular atrophy or amyotrophic lateral sclerosis.

Syringomyelia is characterized by the formation of cavities within the gray matter of the cord and the medulla. Symptoms: Atrophy of the muscles of the hands, arms and shoulders, trophic lesions upon the hands, loss of pain and temperature sense, while the sense of touch is retained or only slightly impaired, motor and sensory symptoms involving various cranial nerves (trigeminus, vagus, hypoglossus).

With **multiple sclerosis** there occur scattered sclerotic areas of degeneration, particularly of the medullary sheathes, together with an increase in the gliomatous tissue in the brain and cord; spastic ataxic gait, intention tremor, nystagmus, scanning speech accentuation of the tendon reflexes,

loss of the abdominal reflexes, psychic disturbances; disturbances of sensibility and of bladder function may be absent but are frequently present. Partial optic atrophy characterized by pallor of the temporal half of the nerve head. Early in the disease sometimes optic neuritis.

With **hemisection of the cord,** e.g., from an injury or tumors, the motility is paralyzed on the same side and the reflexes are accentuated on this side; deep sensibility (muscles and joints) is also lost upon the opposite side; touch is somewhat impaired on both sides but most strikingly so upon that of the lesion. At the level of the lesion, due to the destruction of the root fibers, there tends to be a narrow anæsthetic zone about the same half of the body (**Brown-Sequard hemiparalysis**).

In contrast with the **spinal muscular atrophies** stand the **myopathic dystrophies** in which, though the cord is intact, the muscles are primarily diseased and tend to degenerate. Such myopathic dystrophies begin usually in childhood or in early adult life (hereditary, infantile, and juvenile muscular dystrophies), and involve chiefly the muscles of the shoulder or pelvic girdle together with those of the thighs and lower legs. The disease proceeds often with pseudohypertrophic enlargement of the muscles involved, particularly those of the calf, which show no reaction of degeneration and no fibrillary twitchings.

Abnormally rapid **fatigability** is observed with **myasthenia gravis pseudoparalytica.** This disease is characterized by weakness in the muscles of the face, ptosis, dysphagia and dysphonia, following a brief period of activity on the part of these muscles, which advances to complete loss of function. In the muscles of the extremities the same rapid fatigability is often observed; this may progress to complete paralysis and may be demonstrated by continuous faradic stimulation over a certain period of time during which the electrical irritability gradually decreases (**myasthenic reaction**). After weeks or sometimes years this disease has proven universally fatal; it has never been possible, however, to demonstrate anatomical lesions in the nervous system.

Thomsen's disease (myotonia congenita) is characterized

by an inability of the muscle to relax properly after a strong contraction; the condition of contraction is maintained and only gradually lost. The hand, for example, which has firmly grasped an object, may only be slowly opened by force, or the tightly closed eyelids cannot immediately be opened; all movements are, therefore, performed at first in a slow and lazy fashion, but by repeated performance they become freer and finally normal. Regarding the electrical changes see page 450.

Syphilis may involve the nervous system in adults in several fashions, according as it affects chiefly the meninges, the cerebro-spinal blood vessels, or the parenchyma of the brain, the spinal cord or the nerve roots. Occurs frequently as a **"neuro-recurrence"** in inadequately treated cases. This form of the disease may present all the signs and symptoms of an acute, fulminant inflammation of the meninges at the base of the brain; severe headache, stiff neck and positive Kernig's sign, papillœdema, cranial nerve palsies, sometimes hemiplegia or monoplegia, spinal fluid cell count high. Following adequate treatment (salvarsan) the signs and symptoms may disappear rapidly or completely.

The other lesions produced by syphilis in the central nervous system belong for the most part to the tertiary stage of the disease. **Chronic syphilitic meningitis** producing gummatous infiltration of the leptomeninges, sometimes impinging upon cranial nerves or spinal nerve-roots, is often associated with obliterative endarteritis. The resultant destruction of nerve fibers or brain tissue by inflammation (**myelitis**), or ischæmia, may lead to degeneration of nerves of fiber-tracts. Symptoms and signs vary according to the site and extent of the lesion: Headache, ocular palsies, loss of pupillary reflex to light (Argyll-Robertson pupil), optic neuritis or atrophy, dizziness, hypo- or hyper-reflexia, disturbances of sensibility, hemiplegia, paraplegia or monoplegia, Wassermann reaction in spinal fluid usually positive, blood Wassermann frequently negative.

In **tabes dorsalis** the posterior columns and the posterior roots of the cord undergo degeneration at different levels and to varying extents. In addition there is usually degeneration of certain cranial nerves and their nuclei. Symptoms:

Analgesia and anæsthesia in various segments, most frequently those involving the feet and lower legs, or a girdle-like zone about the trunk and over the inner side of the arm and hand (Th. 1 and 2). Hyperæsthesia for cold on the trunk, lightning pains, particularly in the legs; delay in pain sense, disturbances of deep sensibility, particularly in the legs, sometimes in the hands, producing ataxia, an ataxic stamping gait, swaying with the eyes closed, loss of the knee jerks, ankle jerks and pupillary reflexes, unequal pupils (anisocoria), paralysis of accommodation and of extraocular muscles, girdle sensation, bladder disturbances, attacks of abdominal pain associated with vomiting (gastric crises). Often tabetic arthropathies (**Charcot joints**), e.g., severe deformative processes in the knee, foot and elbow joints which are distinguished by painlessness. The cerebrospinal fluid obtained by lumbar puncture usually shows a small amount of albumen with slight cell increase. The Wassermann reaction in tabes is usually positive in spinal fluid and blood, but may be negative in both.

Friederich's ataxia is an hereditary disease, often attacking several members of a family in the same generation. The symptoms include those of both spinal and cerebellar ataxia: severe ataxia, i.e., of the legs and the trunk, but at times also of the hands, staggering gait, astasia and in addition loss of pupil and tendon reflexes, nystagmus, speech disturbances, talipes cavus and occasionally muscular atrophy of the type of muscular dystrophy. Sensibility usually normal. Anatomical: Degeneration of the posterior columns and atrophy of the cerebellar cortex.

Pernicious anæmia is often accompanied by degenerative lesions in the posterior and lateral columns of the spinal cord. These occasion disturbances of sensibility. tingling in hands and feet, ataxia with loss of muscle sense and vibratory sense; paresis of extremities, tendon reflexes diminished, often absent, occasionally loss of sphincter control.

THE VEGETATIVE NERVOUS SYSTEM

In the central gray matter in the neighborhood of the 3rd and 4th ventricles lies a series of ganglion cell groups, which apparently serve to regulate the more

important vital processes: The maintenance of the **body temperature** is so regulated that upon cooling there is developed an increase in heat production or, with any elevation of body temperature, an increased heat loss is brought about by dilatation of the peripheral blood vessels and by perspiration. Furthermore, the regulation of **water excretion** in the urine is so controlled under the influence of these centers that, with disease of the posterior lobe of the hypophysis, with which they are intimately associated, there takes place an enormous increase in water output in the urine. The administration, in this disease, of normal hypophyseal extract, brings about a conspicuous reduction in the urinary excretion. By means of this central regulation the water content of the blood and tissues is maintained at a normal level. In connection with this the salt content of the blood and tissue fluids is maintained within the osmotic limits of physiological salt solution. If the water content of the blood and the tissues falls below a certain level there develop contractions in the œsophagus which bring about the sensation of thirst. This fine regulation of water and salt content serves the purpose of maintaining a normal osmotic pressure in the blood and tissue fluids, thereby preventing swelling or shrinking of the cells. There is a great deal of evidence indicating that the sugar content of the blood is also regulated by certain nervous centers in this area. If this fall below the normal an increase in the breakdown of glycogen to glucose in the liver is brought about from these centers through the sympathetic nerves and particularly the splanchnics. Furthermore, in the presence of a low blood sugar, contractions of the stomach develop through the action of the vagus, causing the sensation of hunger and demanding relief. In the subthalamic region there is, possibly, another center which acts to regulate the blood pressure, in that, through the activity of vaso-constrictor and vaso-dilator nerves, the diameter of the vessels in various portions of the body is maintained or altered. Finally, it is sometimes assumed that the regulation of sleep and waking is carried out from an area in the thalamus or subthalamic region.

From these vital centers tracts pass to the medulla where there are other vegetative nuclei which regulate respiration,

cardiac rate, water, salt and sugar metabolism. Injury to the 4th ventricle is followed by increased glycolysis in the liver and glycosuria; this phenomenon is produced only if the splanchnics be intact. From the vegetative nuclei in the floor of the 4th ventricle fibers pass via the vagus to the thoracic and abdominal viscera. Stimulation of these fibers leads to contraction of the bronchi and to slowing of the heart rate. From the aorta and the bifurcation of the common carotid centripetal vagus fibers pass upward to the medulla (N. depressor), which, in the presence of an abnormally high blood pressure in the aorta or upon mechanical pressure over the carotid, bring about a reduction in blood pressure and slowing of the heart. The movements of the œsophagus in deglutition and the opening of the cardia are also under control of the vagus. In the stomach the vagus controls peristalsis and the rhythmic opening and shutting of the pylorus as well as the secretion of the gastric juice. In the intestine vagal stimulation causes peristalsis, and with abnormally increased tone may cause the colon to go into spastic contraction resulting in obstinate constipation. The vagus also acts to stimulate the kidneys, bile passages, pancreas and the liver in that it increases the production of the internal secretion of the pancreas (insulin) and causes an increase in the breakdown of glycogen in the liver.

A certain proportion of the tracts from the vegetative centers from the brain and medulla traverse the entire cord to its lower end. Upon the way they receive connections from certain ganglion cell groups in the first dorsal segment, which lie in the angle between the anterior and posterior horns as well as in the lateral horn of the gray substance. From these cells **white, medullated fibers, rami communicantes**, pass outward with the anterior roots to connect with the paravertebral chain of ganglia of the sympathetic. From the cells of the sympathetic ganglia gray, non-medullated fibers (**gray rami communicantes**) connect with the nerves emerging from the cord and course in the mixed nerves to all organs of the body. In addition many of these fibers pass to the walls of the arteries, and as vasomotor nerves, control the constriction and dilatation of the blood vessels, the function of the sweat

glands and other glands, and the movements of the hair upon the skin.

From the stellate ganglion and the inferior cervical ganglion which is connected with it, the paravertebral sympathetic chain passes upward toward the head. In its course it passes through a middle and a superior cervical ganglion and then enters the cranial cavity with the internal carotid artery, where it not only acts to control the diameter of the intracranial vessels in correlation with ever-changing cerebral activity but also furnishes fibers to the ciliary ganglion in the orbit. Through this latter the sympathetic effects dilatation of the pupil. Pressure upon the neck to the point of pain causes dilatation of the pupil; this reflex is absent upon transection of the cervical sympathetic. With destruction of the cervical sympathetic the eye sinks backward into the orbit and the lid slit is narrower. This **Horner's** syndrome is diagnostic of interruption of the cervical sympathetic. Upon the side of a sympathetic lesion there also appears disturbance of the vasomotors and of perspiration over one-half of the face.

The mydriatic action of the sympathetic is antagonistic to the myotic control exercised by the oculomotor nerves. Those fibers of the oculomotor which bring about narrowing of the pupil and accommodation by the lens, i.e., act through the smooth, ciliary muscles, arise in a nucleus which lies at the anterior end of the aqueduct of Sylvius (**Edinger's** nucleus). The smooth musculature of the eye, therefore, is under the antagonistic control of two nerves, the sympathetic and the oculomotor.

From the three ganglia of the cervical sympathetic and from the stellate ganglion sympathetic fibers pass to the lungs and to the heart. Their stimulation brings about acceleration and augmentation of the heart and may sometimes give rise to extrasystoles. In the abdominal viscera, as well, the action of the sympathetic is antagonistic to that of the vagus; it produces vasoconstriction in the vessels of the abdominal organs and intestines, and inhibits the contraction of the stomach, pylorus, intestine and biliary passages, the activity of the kidney and the formation of glycogen. On the other hand, it accelerates the breakdown of glycogen into sugar and in-

creases the production of adrenalin by the adrenals. The sympathetic fibers passing to the abdominal viscera arise as the splanchnic nerves from the cord and paravertebral ganglia at the level of the 6th–9th thoracic segments. They pass for the most part to a large ganglion, solar plexus or cœliac ganglion, which lies just beneath the stomach and in front of the aorta. Into this ganglion there also pass vagus fibers and beyond this point it is impossible anatomically to distinguish vagus from sympathetic fibers. Upon the anterior surface of the aorta, just at the level of the inferior mesenteric artery, lie other **"preaortic"** ganglia which receive fibers from the paravertebral chain in the lumbar region, and from which pass inhibitory fibers to the bladder and sexual organs.

From the lowest portion of the cord, the 3rd to the 5th sacral segments, there passes out with the spinal roots a plexus of fibers, which is distributed as the **pelvic nerve** over the floor of the pelvis and there is connected with a plexus of ganglion cells and nerves. This pelvic nerve or **N. erigens** brings about contraction of the smooth muscle and relaxation of the internal sphincter in emptying the bladder, and controls erection in the male.

The sympathetic nerves in general are opposed by an antagonistic system, the **parasympathetic system**. These parasympathetic nerves course in the oculomotor, chorda tympani, and for the most part, through the vagus, and finally through the pelvic nerves. They all have their origin in the central nervous system. Alterations in tonus of the sympathetic and parasympathetic systems accomplish the delicate regulation of the pupillary diameter, cardiac activity, vascular diameter and functional changes in the bladder and glands which are to be observed in the normal individual. If the parasympathetic influence predominates one speaks of **vagotonus**, if that of the sympathetic is more pronounced, of **sympathicotonus**. It is, however, true that in "nervous individuals" vagotonic and sympathicotonic phenomena are so mixed and complicated that a sharp differentiation is not to be considered. The sympathetic and parasympathetic nerves provide not only efferent paths to the vessels and viscera but also paths for afferent impulses which mediate the sensations of the internal organs. These sensory impressions from the

viscera rarely reach consciousness and then only when the smooth musculature of the stomach, bile ducts, urinary passages, and vessels are brought to a state of cramp-like colic. These afferent paths make possible, however, a series of visceral reflexes which, in part at least, take place in the nerve and ganglion plexuses of the stomach and bladder, i.e., in the intramural nervous system of these organs, but more frequently involve paths through the spinal cord.

The sympathetic nerves and particularly the vasomotors possess also trophic functions. In the case of extreme contraction of an artery the tissues in its domain may suffer so severely from want of blood that the resultant asphyxia may lead to pain or finally to death of the tissue. **Raynaud's** disease is characterized by symmetrical ischæmia of the fingers and toes leading to a cadaverous appearance of the fingers and finally to terrific pains and gangrene of the finger tips. Removal of the vasoconstrictor nerves in the adventitia of the brachial, radial, ulnar, or femoral arteries tends to relieve these symptoms. With lesions of the peripheral mixed nerves vesicles are sometimes formed which frequently leave behind them indolent ulcers; the skin in the affected area is sometimes atrophic, red and glossy. With syringomyelia there sometimes occur changes in the finger nails and deformities or amputations of several phalanges. With tabes and syringomyelia there also sometimes occur pronounced changes in a single joint (arthropathia tabidorum, **Charcot's joint**). With cerebral and spinal paralysis in children the growth of the bones of a paralyzed limb is occasionally conspicuously retarded. Finally, with inflammation of the intervertebral ganglia, which include the Gasserian ganglion of the 5th nerve, there may develop **herpes zoster** in the peripheral domain of the sensory cutaneous nerve involved.

THE EAR

One distinguishes, 1. The outer ear (pinna, external auditory canal and tympanic membrane). 2. The middle ear (tympanic cavity) containing the auditory ossicles, which transmit the vibrations of the tympanic membrane through the stapes to the fenestra vestibuli and thereby to the cochlea. To the middle ear belong also the antrum and cells

of the mastoid process. 3. The inner ear. This contains the sensory organ of hearing (cochlea) as well as the semicircular canals. The latter lie in three planes at right angles to each other corresponding to the three dimensions of space. Through the vestibular nerve they transmit impulses making possible orientation in space, and thereby the maintenance of equilibrium and posture.

In the examination of the auditory canal the pinna is drawn slightly backward and the otoscope introduced. The tympanic membrane is normally a pearl gray color. For purposes of orientation one identifies the small white projection corresponding to the process of the malleus. Above this lies the pars flaccida of the tympanic membrane (Shrapnell's membrane). In the part below the process of the malleus (pars tensa) the handle of the malleus may be identified as a white streak extending to the middle of the tympanic membrane (umbo). In front of and below the umbo there is observed a triangular light reflex. Retraction of the tympanic membrane occurs with closure of the eustachian tube which connects the tympanic cavity with the pharynx; bulging of the tympanic membrane follows exudation in the tympanic cavity, and with inflammation in the middle ear the tympanic membrane is red and swollen. Perforation of the tympanic membrane may take place with inflammation in the middle ear and, with chronic inflammation, such perforation may persist. With Valsalva's test (the patient inflates the cheeks with the mouth and nose closed) or Politzer's test (swallowing with the nose closed) the air may be heard rushing through the perforation in the drum.

In examination of the auditory canal one observes first whether it is patent or full of secretion: wax, pus or blood. Muco-purulent, odorless secretion is found with acute otitis media; thin, usually malodorous, pus with chronic middle ear disease. Swelling or tenderness of the mastoid process, particularly about its point and with traction upon the pinna, indicates an inflammatory process in the mastoid cells.

Functional Test of the Acoustic Apparatus

Whisper test. One tests first the healthy or better ear. The patient closes the other ear by placing the finger firmly

in the outer auditory canal and covers the eyes with the hand. The physician then stands several yards away from the patient and whispers a series of numbers of two figures which the patient repeats as soon as he hears them. If the patient cannot understand these numbers the physician gradually approaches him, determining the distance in meters or centimeters at which the patient can make out all the test numbers. With normal hearing whispered speech may be heard at a distance of 20 and should always be audible at a distance of 6 meters. Among the consonants S and Z and the vowel I in the upper register are best heard, the consonants B, T, P, F, W, D, K, G and the vowels A and E in the middle register, and finally M, R, N, and the vowels O and U in the lower register are best heard. The number 99 is particularly poorly heard with uncomplicated occlusion of the auditory canal, the numbers 5 and 4 with acute middle ear disease, 8 with chronic middle ear disease, 4, 6, and 7 with disease of the inner ear.

For testing with pure tone a tuning fork is used, usually "A" (108 vibrations per second), and "a" (425 vibrations per second). The test is first made with air conduction, by holding the tuning fork a short distance away from the pinna, and then by bone conduction, placing the foot of the tuning fork against the bone of the mastoid process or upon the middle of the skull.

Weber's test. The tuning fork is placed upon the middle of the skull. Under normal conditions the note is heard equally well in both ears. With unilateral disease of the **middle ear** the note is perceived exclusively in the diseased ear, and with bilateral disease in that ear most severely affected. With "central deafness" (**nerve deafness**) due to disease of the 8th nerve or cochlea the note is heard only in the sound ear.

Schwabach's test. With a given tuning fork (A) one compares the duration of bone conduction in the patient with that of a normal individual. If the patient perceives the note longer than the normal the test is positive, if shorter it is negative. With middle ear disease bone conduction is prolonged: with disease of the inner ear it is shorter. With alterations in the skull, e.g., with syphilis or tumors, Schwabach's test is strikingly short or absent.

Rinne's test. Bone conduction is compared with air conduction by placing the foot of the tuning fork (a) first on the mastoid process and directing the patient to indicate when he no longer hears the tone. The tuning fork is then brought before the external canal. If it is heard still longer here one may assume normal conduction in the middle ear. Such a positive result is obtained in individuals with normal hearing but also with central deafness involving disturbances in the nerve or cochlea. If, on the other hand, the note is longer heard with bone conduction than with air conduction it is taken to indicate disturbance in the middle ear. With complete deafness perception by air conduction for the fork "a" is completely lost (Rinne-δ). If only air conduction is perceived it is designated as Rinne + i. The interval over which a note is heard by air or bone conduction is registered in seconds.

Disease processes in the ear may be still further localized by testing with high and low tones by means of the Bezold-Edelmann continual tuning fork series. If, with air conduction, the lowest tones are not heard while the middle and higher tones are well perceived, it is to be assumed that the disturbance is primarily in the middle ear. If, however, the lower tones are heard and the higher not heard, the disease is most probably in the inner ear.

As a rapid method for the certain diagnosis of deafness the test of the affected ear with tuning fork "a" is sufficient. If perception is lost for this note, in the presence of a purulent process in the middle ear, it is highly probable that pus has broken into the labyrinth, a circumstance which greatly favors the development of meningitis. Disease in the inner ear frequently causes tinnitus and vertigo, but it should be pointed out that these symptoms may occur with middle ear disease and with anæmia as well.

Functional Tests of the Labyrinth

Baranyi's test. Cold water (15–25° C.) is injected into the outer ear with a syringe. In healthy individuals there develops nystagmus of both eyes upon looking to the opposite side; upon injecting hot water (45–50° C.) nystagmus upon looking toward the same side. With disease of the labyrinth nystagmus is wanting upon the affected side. Or the patient

is placed upon a rotating table and turned upon his long axis from right to left 10 times in 20 seconds, or he may be simply directed to face about 10 to 20 times rapidly, when standing in the upright position. With a normal vestibular apparatus this procedure is followed by dizziness and horizontal nystagmus upon looking to the right, that is against the direction of rotation, but not toward the left. Upon turning from left to right: horizontal nystagmus upon looking to the left. With disease in the labyrinth dizziness and nystagmus are absent upon rotation toward the side of the diseased ear.

Past-pointing. The examiner holds his finger before the patient and directs him to touch this with his forefinger, at first with the eyes closed and then with them open. The normal individual is able to touch the finger even with the eyes closed; with disease of the cerebellum and vestibular apparatus the patient with his eyes closed points past the finger and tends to do so on the side toward the disease.

The patient is directed to stand with his eyes closed and feet together, to turn the head toward one side and to drop the shoulder on that side. With normal vestibular apparatus the patient tends to sway to the side toward which the head has been turned. With disease of the vestibular apparatus or cerebellum this sign is absent or indefinite. Finally, following unilateral disease of the vestibular apparatus, there persists for some time a tendency in walking to deviate from a straight line toward the side of the affected labyrinth, or even to fall in that direction.

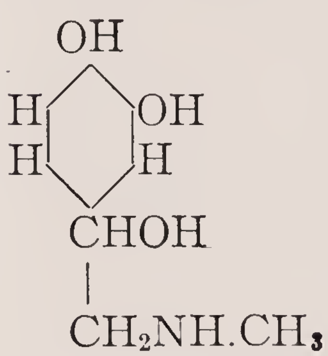
With lesion of the semicircular canals **Meniere's syndrome** frequently develops: Attacks of violent vertigo with the illusion that objects are moving in one of the three dimensions of space, frequently associated with nausea, vomiting, slowing of the pulse and tinnitus.

Middle Ear Disease	Test	Inner Ear Disease
Not well heard.	Low tones.	Normal, deep tones well heard.
Normal high tones better heard.	High tones.	Not well heard.
Note heard exclusively, or better, in diseased ear.	Weber-Schwabach.	Note shortened and referred to normal, or better ear.

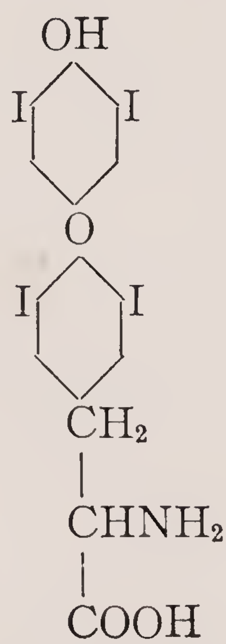
CHAPTER IX

THE GLANDS OF INTERNAL SECRETION

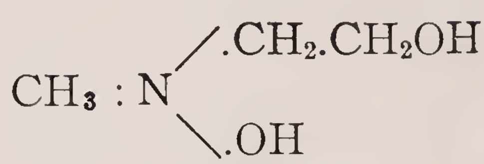
To THE glands of internal secretion belong the thyroid, the parathyroids, which lie in pairs just behind the lower pole of the thyroid, the thymus, the adrenals, the sexual glands (testes and ovaries), the hypophysis, the pineal gland, and, finally, the pancreas. Some of these glands have no ducts and secrete their products directly into the lymph and blood vessels, others, the testes and the pancreas, possess ducts which carry away certain other products or secretions; still another variety of such glandular tissue is distributed among various internal organs. The secretions of these so-called "endrocrine glands" are known as "hormones," since they bring about the harmonious interactivity of other organs at a distance. The chemical nature of certain of these hormones is now known, i.e., the product of the adrenals, adrenaline, as well as thyroxine from the thyroid, and choline, the hormone of the intestine.



Adrenaline



Thyroxine



Choline

The glands of internal secretion act principally upon the metabolism, e.g. carbohydrate metabolism; they also influence the nutrition of the organism, and, in young individuals,

development and growth. These glands are intimately related to the vegetative nervous system, i.e., those nerves which, independently of consciousness, control the various vital processes of the body. Not only are they all controlled by the vegetative nervous system but their secretions exert a stimulating or depressing influence upon it.

Hypofunction of the endocrine glands may be observed in such diseases or experiments in which, either through operation or disease, such a gland is removed or atrophied. Or one may regard those symptoms, which result from hypertrophy or abnormally profuse blood supply to such a gland or from the injection of glandular extract, as indicative of hyperfunction. It is highly probable that, in addition to hypofunction and hyperfunction of such glands, there exists a condition of dysfunction involving qualitative changes in the glandular activity. It is to be noted that these glands are functionally interrelated in a complex fashion which makes most difficult a clinical study of the function of a single gland.

Thyroid. The thyroid is a glandular organ composed of vesicles lined by an epithelial secretory membrane and normally containing colloid material. This colloid contains thyreoglobulin and thyroxine, the active principle of the thyroid gland. Subcutaneous injection of thyroxine produces results identical with the administration of dried, pulverized thyroid gland by mouth, i.e., augmentation of metabolism. Since thyroxine contains a relatively large proportion of iodine a certain, though minimal, supply of iodine in the food is necessary for its production. In certain districts the prevalence of goiters containing large amounts of colloid is apparently associated with deficiency of iodine in the food and water supply. Such goiters are usually not accompanied by symptoms of hyperthyroidism, rather the reverse. Too rapid administration of iodine in such cases may lead to an overproduction of thyroxine with symptoms of Basedow's disease.

Hypofunction. If the thyroid be completely removed by operation, or so much of it be extirpated that the remainder is unable to function adequately there results a serious condition of degeneration and cachexia: Puffy, yellowish appearance of the face and upper body, lips swollen, tongue thickened, alopecia, finger nails coarse, skin generally dry,

body temperature subnormal, subjective sensation of cold, basal metabolic rate reduced to 20–40% below the normal, general lassitude, bradycardia, constipation, dull mentality. If the thyroid gland atrophy following an inflammatory process a similar disease picture is produced, which, on account of the puffy appearance of the patient, is known as **myxœdema.** The development of severe thyroid insufficiency in early childhood or before adolescence results in impairment of development of the bones such that the epiphyses persist into adult life. The individual remains small, the limbs are plump, the bridge of the nose is sunken and umbilical hernia is frequently present. The mental development of such individuals is conspicuously retarded. This condition is known as **cretinism** and appears sporadically or endemically in regions where goiter is endemic. In the majority of cretins there is a nodular goiter in which outspoken areas of degeneration may be demonstrated. In the most severe cases, associated with idiocy, the thyroid is sometimes altogether absent. Cretinism is sometimes associated with serious impairment of hearing or deafness and, when this appears in childhood, the patients are also mute.

Hyperfunction (hyperthyroidism and Basedow's disease). Thyroid usually enlarged, soft; strong pulsation, palpable thrill and audible bruit over the gland, indicating increased blood supply; the symptoms of hyperthyroidism may appear when a previously enlarged thyroid is rapidly decreased in size by the action of iodine or X-ray: Tachycardia, palpitation, forceful cardiac action, frequently with a systolic murmur at the pulmonic area. The simple tachycardia may in time progress to an irregularity; extrasystoles, paroxysmal tachycardia, or auricular fibrillation, or finally to dilatation of the heart and myocardial insufficiency. Mild elevation of body temperature, subjective feeling of warmth and profuse sweats point to elevation of the oxidative processes in the body. Corresponding to this the carbon dioxide output and the oxygen intake may be elevated to 30–80% above the normal; the patients tend to lose weight despite a ravenous appetite, and high caloric diet. Alimentary glycosuria. Increase in the lymphocytes in the blood up to 30–60% of the white blood corpuscles (8). Falling out of the hair, suppression of the secondary sex characteristics, decrease in sexual function. Fre-

quently violent diarrhœa as a result of accelerated intestinal peristalsis, tremor of the hands, emotional instability, brownish pigmentation about the eyes. The eyes themselves appear glistening and staring; the upper lid tends, upon quick fixation of the glance upon an object, to be raised upward and to follow with a lag any downward rotation of the eye, so that above the upper corneal margin a white strip of sclera remains visible (Græfe's sign), infrequency of winking (Stellwag's sign), inability to converge both eyes upon the same object (Mœbius). In protracted and fully-developed cases exophthalmos. In the strict sense of the word the diagnosis of Basedow's disease should be restricted to those cases in which, in addition to struma and other symptoms of hyperthyroidism, there are also present exophthalmos and the characteristic eye signs described above. In women hyperthyroidism is frequently associated with the presence of myomata uteri.

Parathyroids. Hyperfunction. (Barr, Bulgar and Dixon, and Albright, Aub and Bauer have reported cases of hyperparathyroidism with parathyroid tumors or hyperplasia. The blood calcium is high and the phosphorus low: the excretion of calcium in the urine is increased so that metabolic studies show a negative calcium balance. Associated with this are rarefaction of bone, muscular weakness and hypotonia, and calcified urinary calculi. Removal of the tumor restores the calcium metabolism toward the normal and relieves the symptoms. Ed.)

Hypofunction. Not infrequently, following an operative procedure in the neck, e.g., thyroidectomy, a large proportion of the parathyroid tissue is destroyed or injured, or its blood supply is seriously impaired. There develop following this, spasmophilia and **tetany:** Increased irritability of the vegetative nervous system, intestinal spasm, attacks of cramp-like tonic contractions in the fingers, arms and face and sometimes in the legs, increased irritability of the motor nerves to percussion, pressure, and galvanic current, Chvostek's and Trousseau's signs (see page 448), defects in dental enamel, cataract, disturbances in the calcium metabolism. Parathyroid insufficiency is particularly apparent in women in pregnancy and at the time of the menses.

(**Collip** has prepared an extract of the ox-parathyroid

[Parathormone] which may be administered by hypodermic injection. In the normal it brings about an elevation of blood calcium and a fall in blood phosphorus. Overdosage causes an excessive rise in blood calcium, and anuria; at the same time the blood phosphorus and non-protein nitrogen rise as uræmia develops. The primary action of this extract is not clear; it may directly, or indirectly through lowering of the phosphorus, result in a mobilization of calcium from the bones into the blood. In addition it may possibly affect the absorption of calcium from the intestine. Administered to cases of post-operative or idiopathic hypoparathyroidism, parathormone causes a rise in blood calcium, a fall in blood phosphorus, and relief of the associated tetany. In infantile tetany the phosphorus is lowered slightly, the calcium is raised, and spasmophilia is relieved by injection of the extract. Ed.)

(Ellsworth and Albright studied a case of idiopathic hypoparathyroidism in a boy of 16 years. Blood calcium was low; blood phosphorus high; calcium excretion in urine low, that of phosphorus normal. The patient suffered from tetany and showed incipient cataracts. Parathormone caused the tetany to disappear; blood calcium rose and phosphorus fell; urinary phosphorus immediately increased; calcium output in the urine remained low until blood calcium reached 8.5 mg.% when it suddenly rose. Ed.)

Tetany may, however, make its appearance in children and in adults without demonstrable anatomical lesion of the parathyroids, e.g., with gastrectasia due to profuse vomiting, the loss of large quantities of acid with the acid gastric contents, and resulting **alkalosis.**

The **thymus,** which in children occupies a considerable space beneath the upper end of the sternum and above the heart, is composed chiefly of lymph follicles but contains peculiar epithelium-like cells. It tends to atrophy at or before puberty leaving only a lappet of fat containing only occasional glandular rests. An abnormally large thymus (thymus hyperplasia) is not infrequently observed in children who have suddenly died without other demonstrable cause, or have shown a strikingly low resistance to infectious diseases. With such thymus hyperplasia there is often associated the so-called status lymphaticus, i. e., hyperplasia of all lymphatic tissue

in the pharynx, tonsils, lymph nodes, as well as of the Peyer's patches, and the solitary lymph follicles of the intestine. This condition presents a peculiar constitutional anomaly and usually becomes apparent in the second decade of life. In Basedow's disease the thymus is almost always hyperplastic and is occasionally so in myasthenia gravis pseudoparalytica. It is possible that the thymus stands in some relation to the normal processes of growth during the early years of life and particularly to that of the bones. With premature atrophy of the thymus growth ceases; this may lead to **thymogenic dwarfism** and to abnormal fragility of the bones.

The **adrenals,** which lie on either side at the upper pole of the kidney, develop in two portions, the mesodermal cortex, and the ectodermal medulla. The function of the cortex, which is made up of fat-containing cells, is still unknown but seems to be related to the development and function of the sexual organs. With pathological processes in the cortex premature development of the genitalia and of the secondary sex characteristics (change of voice and beard) has been observed (pubertas præcox). The medullary tissue is richly supplied with sympathetic nerves and ganglion cells and contains other cells which stain yellowish-brown with the salts of chromic acid. These **"chromaffin cells"** are found not only in the adrenal medulla but are distributed about the ganglion masses of the sympathetic system in the abdomen; they are grouped under the term chromaffin system. From the adrenal medulla there has been isolated an active crystalline substance, adrenaline, which, like thyroxine, may now be prepared synthetically. Injection of adrenaline produces local and generalized vascular constriction and leads to a rise in blood pressure. The coronary arteries alone are dilated thereby in contrast to the other arteries. Injection of adrenaline also brings about hyperglycæmia and glycosuria due to the fact that the liver glycogen is rapidly broken down into sugar. Adrenaline stimulates contraction of the uterus and inhibits the contraction of the bronchial musculature. The injection of ¼ to 1 c.c. of a 1:1000 aqueous solution of adrenaline relieves the bronchial spasms of asthma; the abnormally inflated lung is thereby diminished in size. **Hyperfunction** is

not clinically recognized and it is extremely doubtful whether any protracted abnormal elevation of blood pressure, such as is observed with renal disease and arteriolar-sclerosis, bears any relation to this condition.

Hypofunction. With bilateral atrophy or degeneration of the adrenals, e.g., as a result of tuberculosis, there results the picture of **Addison's disease:** Cachexia, muscular weakness, complete anorexia, suppression of gastric secretion, vomiting, diarrhœa, hypotension, striking hypoglycæmia with increased sugar tolerance, i.e., absence of alimentary glycosuria following liberal ingestion of sugar, brownish pigmentation of the skin and mucous membranes, death from exhaustion.

The **sexual glands (testes and ovaries)** undergo rapid development at puberty. At the same time the secondary sexual characteristics, both mental and physical, become manifest. In the male the penis, testes and prostate increase in size, the voice deepens, the beard grows rapidly and the musculature of neck and body develops. In the female the uterus and breasts enlarge, and the pelvis broadens. In both sexes the axillary and pubic hair appears. In the female the crines pubis stops in a horizontal line over the mons veneris but in the male extends upward as far as the umbilicus. The development of the secondary sexual characteristics is coincident in both sexes with the attainment of adult stature. The epiphyses of the long bones close and growth ceases soon after sexual development becomes complete.

In case the testes and the ovaries fail to undergo their normal development, or if they are removed prior to puberty by castration, the secondary sex characteristics fail to evolve (infantilism). In the female this is characterized by underdevelopment of uterus and breasts, a narrow pelvis, boyish instincts, and stronger musculature, and sometimes amenorrhea; in the male the penis and prostate remain small, the beard does not develop, the voice remains high-pitched and sometimes there occurs a distinct enlargement of the mammary gland. In both sexes the axillary and pubic hair is scant or absent. Furthermore, growth tends to continue, especially in the extremities, so that arms and legs become disproportionately long in comparison to the body. Certain psychic anomalies may also occur, among them homosexual tendencies.

In the normally-developed female the onset of menstruation (menarche) appears between the twelfth and sixteenth years: thereafter menstrual periods occur normally every four weeks and last about five days each. At about the 50th year menstruation ceases as the ovaries cease functioning and atrophy. This menopause (climacteric) is sometimes accompanied by obesity and change in temperament.

In the adult female menstruation ceases during each pregnancy, and for six weeks thereafter, or during the period of lactation. The development and function of the uterus are directly dependent on the ovaries, and in fact on the maturation of the ovum. In the ovaries there are, in addition to the interstitial cells, a large number of primordial follicles (primordial ova). Every four weeks in the human female one of these (in the case of duplicate twins, two) develops into a mature Graafian follicle. By specific proliferation of the follicular epithelium, and the formation of liquor folliculi, there is formed a vesicle, in the wall of which the ovum is imbedded. This follicle increases in size, is extruded to the surface of the ovary, and bursts. The fluid contents of the follicle are emptied into the abdominal cavity; the ovum passes into the orifice of the Fallopian tube and is conveyed into the cavity of the uterus. Under the influence of the fluid contents of the follicle the mucous membrane of the uterus and vagina undergoes extensive proliferation. If the ovum is not fertilized it perishes; hyperæmia and hypertrophy of the epithelium of the uterine mucous membrane occur and menstruation begins. The rupture of the Graafian follicle occurs about midway between two menstrual periods.

Experiments on animals have confirmed the effect of the follicular fluid on the development of the glandular epithelium of the uterus and vagina (œstrus). These studies have also led to the isolation of a specific substance (folliculin). If folliculin be injected into a female rat or mouse before puberty the premature maturation of an ovum takes place and œstrus occurs, as manifested by hyperæmia, proliferation and exfoliation of the vaginal mucous membrane. Œstrus may also be produced in the castrated adult female mouse by the injection of folliculin; this procedure affords a biological test for the presence of folliculin in any fluid (e.g., blood).

Following the bursting of the Graafian follicle its walls collapse; soon it becomes filled with cells containing a yellow pigment and at this stage is known as the corpus luteum. Its subsequent history appears to depend upon the fertilization of its liberated ovum. If fertilization fails to take place the corpus luteum reaches its maximum size within about two weeks and is then slowly absorbed. If, on the other hand, fertilization does occur the corpus luteum persists and enlarges, and appears to exert a considerable influence upon the fixation of the ovum in the uterus, at the same time inhibiting ovulation during the pregnancy.

The **hypophysis** lies in the sella turcica covered by the dura. It is composed of several portions which appear to have entirely different functions. The anterior lobe, which develops as a diverticulum from the roof of the pharynx, is of a glandular structure. The posterior lobe is connected by a stem with the infundibulum of the third ventricle; it receives countless nerve fibers from the subthalamic gray matter and shows a glial structure. Near the stem are found the pars intermedia and pars tuberalis, whose functions are not yet known.

If the entire hypophysis is removed from young animals growth ceases. If, over a long period of time, the extract of the anterior lobe is injected into young rats or, if an anterior lobe is implanted into them, growth is stimulated. This growth-promoting effect is found only in the anterior lobe and the extract therefrom.

Hypertrophy or hyperfunction of the anterior lobe results, in young individuals, in excessive growth of the skeleton (gigantism). If, however, hyperfunction takes place in later life at a time when the epiphyseal lines are united and growth of the long bones is no longer possible there ensues **acromegaly,** characterized by periosteal growth and disproportionate increase in size of the hands and feet, nose, lips, tongue and lower jaw, and, often, increase in the antero-posterior diameter of the thorax. Usually impotency occurs in the male, and sterility and growth of beard in the female. Hypophyseal enlargement may be recognized in a lateral X-ray of the skull by the resultant enlargement of the sella turcica. Pressure upon the optic chasm by an hypophyseal tumor results in bitemporal hæmianopsia; this is accompanied by headache

as a result of increased intracranial pressure. Furthermore sugar is often found in the urine under these circumstances suggesting that, directly or indirectly, the pituitary gland influences carbohydrate metabolism.

Atrophy of the anterior lobe leads to "hypophyseal cachexia," which is characterized by excessive general loss of weight and dimunition in size of various organs, particularly the sex organs.

The growth-promoting effect of the anterior lobe of the hypophysis has an especial influence on the sexual glands in both sexes. Under the stimulation of the hypophysis at puberty the testicles and ovaries mature. Injection of extract from the anterior lobe of the hypophysis produces in immature male animals a sudden development of the testicles and sexual impulse; in immature female mice and rats there occurs a few days after the injection of extract from the anterior lobe an enlargement of the ovaries and development of Graafian follicles accompanied by œstrus. The vaginal epithelium undergoes a significant thickening, and numerous cast-off epithelial cells are found in the vaginal secretion. In animals whose ovaries have been previously removed by operation the injection of this anterior-lobe extract (prolan) does **not** bring on œstrus in the uterus and vagina. The extract from the anterior lobe of the hypophysis appears, therefore, to exert its action only through the gonads, as contrasted with folliculin (see above) which produces œstrus in castrated animals. Folliculin and prolan may be further distinguished by the fact that the former survives boiling and may be extracted with ether.

Aschheim and Zondek have proved that the œstrus-producing substance of the anterior lobe of the hypophysis, as well as folliculin, is to be found in considerable amounts in the urine of women during the entire course of pregnancy. This observation has afforded a diagnostic test for pregnancy.

The pregnancy test is made in the following way: 50 c.c. of the urine (morning) of the woman in question is filtered and extracted with ether (to remove the folliculin). The ether extract is discarded and the urine, after removing the last traces of ether, is injected in about 6 doses of 0.3 cc. in the course of 3 days into 5 young (3 to 4 weeks old) mice weighing

6–8 gm. Three days after the beginning of the injection the occurrence of œstrus is manifested by the characteristic exfoliation of vaginal epithelium. Ninety-six hours after the first injection the mice are killed. The typical positive reaction (pregnancy) is manifested by appearance of spots of blood and countless yellow bodies in the enlarged ovaries of the mice so treated.

From the posterior lobes of the hypophysis and the adjacent parts of the infundibulum are obtained extracts which are called hypophysin, pituitrin, coluitrin or "pituglandol." Injection of these extracts has the same effect on animals as on man, e.g., a significant reduction of the urinary excretion and consequently a retention of water and salt in the organism. Removal of the **entire** hypophysis causes in animals an abnormal urinary output analagous to diabetes insipidus in man. In cases of diabetes insipidus 2–3 daily injections of extract of the posterior lobe suppresses the abnormal urinary excretion and relieves the insatiable thirst from which such patients suffer. In the posterior lobe of the hypophysis and its surrounding tissue it appears that substances are formed which influence the salt and water content of the whole body and affect the function of the kidneys. Also injection of extract from the posterior lobe causes an increase of the blood pressure (vasopressin, pitressin). With tumors in that region the blood pressure is sometimes observed to fall from 60–30 mm. Hg. Finally, the extract from the posterior lobe affects the musculature of the intestine, uterus and gall bladder, causing it to contract.

The disease picture of **dystrophia adiposohypogenitalis** (Frölich syndrome) was previously supposed to depend upon disease of the middle lobe. Recently it has seemed improbable that this disturbance of development is in any way connected with the hypophysis. It occurs in young individuals from 10–20 years of age, and is characterized by obesity, knock-knees and under-development of the testes or ovaries and of the secondary sex characteristics (hypogenitalism). In many cases a normal sexual development results although considerably delayed.

The **epiphysis,** or pineal gland, lies immediately above the anterior corpora quadrigemina and normally undergoes

involution at about the time of puberty. Destruction of the pineal body by tumors during childhood leads to precocious development of the sexual organs and secondary sex characteristics.

Pancreas. In addition to trypsin, lipase and diastase, (digestive ferments) the pancreas elaborates an internal secretion, insulin, which is secreted directly into the blood stream. Insulin, which may be extracted from the gland with alcohol, enhances the accumulation of glycogen in the liver and reduces the blood sugar. It enhances also the utilization of sugar throughout the organism. It is therefore an effective remedy in diabetes.

If too large amounts of insulin be injected into a patient the consequent rapid disappearance of sugar from the blood may be accompanied by alarming symptoms: sweating, syncope, coma and convulsions, which may be relieved almost at once by the administration of sugar, orange juice or chocolate. With operative removal of the pancreas, or with atrophy or degeneration of any considerable portion of the gland, diabetes mellitus results, the blood sugar increases conspicuously and the liver is no longer able to store glycogen.

CHAPTER X

METABOLISM AND NUTRITION

In the living human organism there is continually taking place the destruction and combustion of higher organic compounds whereby energy is freed for the production of heat and work. In the glands secretions and hormones are elaborated, secreted and utilized, and these substances also contain complicated organic compounds. The cellular tissues are constantly undergoing renewal as the older elements (e.g., blood corpuscles) are broken down and replaced. In order to replace materials as they are utilized, and to maintain the body in its normal condition, appropriate foodstuffs must be ingested in sufficient amounts in the diet. Those substances above all are indispensable which maintain the nutrition of the body: **proteins, fats,** and **carbohydrates**.

In addition to these foodstuffs, the burning of which serves to make available to the organism the energy necessary for the maintenance of life, certain other substances are indispensable to the body structure, to its growth, and, above all, to the maintenance of health: Certain inorganic mineral substances (salts), which are contained in more or less complex compounds in the organ and tissue juices (e.g., alkalies, calcium, magnesium, chlorine, sulphur, and phosphorus-containing compounds as well as iron and traces of iodine), and certain organic substances, as yet not accurately identified, contained in rice, in fresh vegetables, in the yolk of eggs, in butter and in meat. These complementary substances are known as **vitamins**, and if they are lacking in the food, the health of the individual suffers and malnutrition may be evident: Loss of weight, œdema, infirmity, nervous paralyses, and, in young individuals, interference with growth.

Among the **vitamins**, in the strict sense of the word, are distinguished two classes: Fat-soluble and water-soluble.

Stepp has demonstrated that animals cannot be kept alive upon a diet which is completely free of fat, i.e., that the fats contain certain materials essential to life. Among these

fat-soluble vitamins animal experimentation has led to the differentiation of **vitamin A**, whose absence leads to standstill of growth, softening of the cornea (xerophthalmia) and finally to the loss of the eye. This vitamin is insoluble in water, thermostabile, and is contained in cod-liver oil and, in varying amounts, in milk, butter, egg-yolk and certain plants. It is absent from potatoes, and from vegetable fats and oils. Closely related is the fat-soluble **vitamin D**, lack of which causes a disturbance in the calcium metabolism producing the disease picture of rickets. This vitamin is also contained in considerable quantities in cod-liver oil, in egg-yolk and in the butter fat derived from cows which have received fresh green food. Alfred Hess and Windaus have shown that this important antirachitic vitamin is closely related to cholesterine (and particularly to ergosterine) and is formed upon exposure to sunlight or ultraviolet light. Evans differentiates further a fat-soluble **vitamin E**, lack of which leads to disturbances in fertility, and, specifically, to testicular atrophy and abortion.

Among the **water-soluble vitamins** are the **antineuritic vitamin B** and the **antiscorbutic vitamin C**. In the orient there is encountered a disease known as **beriberi** which is characterized by progressive paralysis (polyneuritis), tachycardia (vagus paralysis), œdema and disturbances of nutrition. Eijkman has shown that this disease is brought about by a diet composed exclusively of polished rice and that it may be so reproduced in fowls and pigeons. The addition to the diet of the rice hull, egg-yolk, potato, yeast or the juice of fresh green vegetables has been shown by C. Funk to prevent the development of paralysis. This vitamin, necessary to the normal function of the nerves, is absent from hulled rice, pure white meal or muscle tissue. It is abundant in all plant embryos, in rye flour, in potato, egg-yolk, carrots, tomatoes, oranges, and in small amounts in the milk of grass-fed cows.

It has long been known that elimination of fresh vegetables from the diet brings about scorbutus or **scurvy**, with bleeding gums, hæmorrhages in the subcutaneous tissue and musculature, and severe undernutrition. By the administration of fresh vegetables scurvy is cured. **Antiscorbutic vitamin**

C is contained in all fresh vegetables, in potatoes, tomatoes, oranges and lemons, and in the milk of grass-fed cows. It is absent from muscles and bread, and, since it is rapidly destroyed by heat (pasteurization) and by oxygen, it is absent from all preserves and from pasteurized milk. In children deficiency of this vitamin leads to Mœller-Barlow's disease characterized by hæmorrhage in the mucous membranes and beneath the periosteum. Among the avitaminoses should perhaps also be classed **pellagra** which is observed to develop following a diet restricted to corn meal.

In the normal individual it is immaterial, within wide limits, whether the energy requirements of the body be furnished by protein, fat, or carbohydrate, since, as far as heat production is concerned, these materials can replace one another. It is only important that a certain minimum of protein be ingested. As the unit of heat production is employed the (large) calory, i.e., the amount of heat required to raise the temperature of one kilogram of water 1° C (from 14.5–15.5°).

As was originally demonstrated by Rubner the various foodstuffs by their combustion in the body produce the following amounts of heat:

1 gm. protein	4.1 cal.
1 gm. fat	9.3 cal.
1 gm. carbohydrate	4.1 cal.

and their isodynamic amounts (producing equal amounts of energy), are as follows:

100 gm. fat—211 gm. protein—232 gm. starch or 234 gm. sugar.

The rate of metabolism in the normal individual is dependent (1) upon the amount of heat necessary to maintain the normal body temperature and (2) upon the work actually performed. Under the term work is to be included not only that expended in muscular exercise but also that involved in the performance of physiological functions, i.e., the maintenance of the circulation (cardiac work), respiration, glandular activity, digestion and absorption, etc.

The metabolism of different individuals, therefore, varies;

it is greater in a strong, large man than in a small, weak one, greater in men than in women, and in children, relative to the body weight, greater than in adults. Muscular activity is the fundamental factor in this regard and the laborer may require twice as much energy as an individual engaged in a sedentary occupation. On the other hand, mental activity causes no conspicuous increase and the requirements under these conditions are by no means as great as those of a more active individual.

The energy requirements in a healthy adult man at absolute rest in bed and fasting amount to about 1 cal. per kilo body weight per hour, i.e., for a body weight of 70 kilos, 1600 to 1700 calories per 24 hours. For smaller men and for women it is correspondingly lower (for 50 kilos about 1200 cal.), and for heavier individuals greater. This energy requirement under conditions of complete rest and fasting is known as the **basal metabolism.**

The basal metabolism may be more accurately calculated upon the basis of body surface rather than body weight; the normal requirement is about 34.7 cal. per square meter per hour. The body surface may be calculated by Meh's formula $O = K \sqrt[3]{P^2}$ in which O is the body surface in square meters, P the body weight in kilograms and K a constant: 12.3. DuBois utilizes in his calculations the body surface and the body length in centimeters (L) according to the following formula: $O = P^{0.425} \times L^{0.725} \times 71.84$ and finds the basal requirements to be 39.4 calories per square meter per hour. The basal metabolism is estimated by measuring the oxygen consumption at complete physical and mental rest and not less than 12–15 hours after the last meal. The patient inspires for a definite period from a vessel filled with oxygen; the expired CO_2 is absorbed by soda lime. The quantity of oxygen in the vessel decreases with each respiration by exactly the amount which is absorbed in the lungs. By means of a pen the spirometer is caused to record upon a rotating drum for a period of about 10 minutes. This record is then compared with the oxygen consumption of a normal individual of the same sex, weight, height and age according to tables compiled by Benedict and by DuBois and based upon a large

number of observations upon normals. A pathological increase in basal metabolism up to 30–80% above normal occurs in fever and particularly in hyperthyroidism (leukæmia —Ed). Decreased basal metabolism (15–30% below normal) occurs in hypothyroidism and in many forms of asthenia. [The method described above yields falsely high values in any condition associated with cyanosis, e.g., circulatory failure. Under these circumstances, depending upon the degree of oxygen-unsaturation in the blood, a certain amount of oxygen is absorbed in addition to the normal metabolic requirements. Ed.]

The ingestion of food increases the metabolic rate by 10–12% per 24 hours and this increase is far more striking in the case of protein food than in that of carbohydrate or fat, a fact which Rubner designated as the "specific dynamic action" of the foodstuffs. The metabolic requirements under conditions of limited activity or predominantly sedentary work amount to 2300–2500 calories per 24 hours, with moderate bodily exertion 3000, and with vigorous muscular work 3500–4000, rarely more. Small and weak individuals, or those who are severely undernourished may be maintained in metabolic equilibrium at rest with 1300–1500 calories. In children the metabolism, and at the same time, nutritional requirements, are, in toto, less than in adults, but greater in proportion to body weight. An infant requires, during the first half year of life, 300–700 calories per day or 80–100 calories per kilo body weight, and a boy of 6–10 years about 60 calories per kilo.

Nutritional Requirement per diem (after C. Voit)

	Protein	Fat	Carbohydrate	N.	C.	Cal.
Laborer weighing 70 kilo (154 lbs.)	118	56	500	19	320	3054
Professional man (physician)	127	89	362			2833
Prisoner	87	22	305			1812
Average	85	65	465			2876

Energy Requirements (per hour) of a 70 kilo (154 lb.) man. (After N. Zuntz)

Absolute bed rest	70 cal. (basal metabolism)
Standing at "attention"	80 cal.
Walking on level (2 mi. per hr.)	210 cal. (basal + 140)
Marching on level (3.5 mi. per hr.)	350 cal. (basal + 280)
Mountain climbing (ascending 300 yds. at 2 mi. per hr.)	360 cal. (basal + 290)
Mountain climbing (ascending 500 yds. at 2 mi. per hr.)	500 cal. (basal + 430)
Bicycling (8.8 mi. per hr.)	380 cal. (basal + 310)
Swimming	640 cal. (basal + 570)

The rate of metabolism in the organism, i.e., the combustion of available material, is dependent primarily upon the functions and requirements of the body, and is influenced conspicuously by muscular activity; it is, on the other hand, independent of the ingestion of food. In the healthy individual the taking of food is regulated much more by the appetite, not only in a quantitative sense, in that this indicates how much must be eaten to meet the energy requirements, but also in a qualitative sense, in that it leads to the choice of such foodstuffs as are necessary for the maintenance of equilibrium and the normal functions of the body, e.g., vitamins.

If an individual take less food than is necessary to meet the requirements of heat production and work, a portion of his own body tissue, and above all fat and muscle-protein, is consumed and burned. The fasting human being lives only at the cost of his own tissues and the rate of combustion is only slightly less (1500–1850 calories) in the fasting than in the nourished individual.

If, on the other hand, larger quantities of foodstuffs are ingested than are necessary to the maintenance of metabolic equilibrium the greater part of this excess remains in the body and is stored. Since only relatively small quantities of protein can be stored by adults, and only a few hundred grams of ingested carbohydrate may be stored as glycogen in the liver and the muscles, and since excess of carbohydrate may be converted into fat, this excess is principally stored in this

form (in the subcutaneous connective tissue, about the kidneys and in the omentum).

Whether an individual gains or loses upon a given food intake is best determined by following his body weight. This is, however, not absolutely accurate inasmuch as the body weight may remain the same upon a lower food intake if more water be absorbed; the body weight also increases with any accumulation of exudate, effusion or œdema and falls when such effusions are absorbed. Profuse perspiration may cause a transient fall in body weight of 1–2 pounds. One liter (1 quart) of water weighs approximately 1 kilo (2.2 pounds).

Since, in the human body, there is a continual transformation and combustion of structural protein (even with entirely adequate fat and carbohydrate intake), a certain definite amount of protein must be ingested which cannot adequately be replaced by other foodstuffs. The smallest amount of protein upon which the normal conditions of the body can be maintained is known as the **maintenance protein**. This amount, i.e., that necessary to maintain nitrogen balance and to compensate for any considerable loss of protein, varies somewhat according to the amount of other substances (nitrogen-free), i.e., fats and carbohydrates, which are ingested with the food. In the usual diet there are about 50–120 gm. protein (8–20 gm. nitrogen). With abundant administration of carbohydrate and fat the body may do with 22–30 gm. protein (3.5–5 gm. nitrogen), i.e., such amounts may, under these circumstances, be sufficient to maintain nitrogen equilibrium, but it is extremely doubtful whether such a low protein diet may be taken over a long period without injury to health. If, with abundant carbohydrate and fat in the diet, the protein be reduced to almost zero, 2.5–3.5 gm. nitrogen (0.04–0.05 gm. per kilo) are still excreted in the urine, representing a daily protein metabolism of 15–21 gm. (Landergrin and Rubner.) The nitrogen-free substances, namely fats and above all carbohydrates, have the property of **sparing the protein** by suppressing the protein metabolism. In complete starvation the nitrogen excretion in the urine and stool is conspicuously greater due to the consumption of the body fat and protein to meet the

energy requirements; this amounts in the first few days of fasting to 10–13 gm. N (representing a loss of protein of 65–80 gm.), falls during the first two weeks to 6–8 gm. N–37 gm. protein, and, in a long fast, sometimes still lower. If more protein be furnished in the diet than is necessary to the maintenance of metabolism more is utilized, since, of all the foodstuffs which are absorbed from the intestine, protein is the first to be utilized, and the body rapidly comes into nitrogen equilibrium, i.e., as much is burned as is absorbed. The body possesses wide adaptability as regards maintaining nitrogen equilibrium upon the most varied protein intake, as long as this does not fall below the maintenance minimum; even with the greatest protein intake there occurs little or no increase in the protein content of the body. Aside from the **protein intake** the breakdown of protein in the body is dependent also upon the protein content of the organism so that a muscular laborer requires larger amounts of protein in the food to maintain the stability of his body protein than does a convalescent patient. **Bodily exercise, on the other hand, has little or no influence upon the degree of protein breakdown,** i.e., the laborer breaks down no more protein in a working day than in a resting day; on the working day, however, the other processes of combustion, i.e., the oxidation of fats and carbohydrates are conspicuously increased.

Permanent **storing of protein** may not be accomplished in the healthy adult by increasing the protein intake alone, but may be effected by the administration of a diet not only rich in protein, but containing also large quantities of fat and of carbohydrate, which act to spare protein. However, such storing of protein is usually insignificant and, upon return to the customary diet, is soon lost. A more significant and lasting storing of protein, i.e., retention of the protein absorbed from the food, takes place only in young, growing individuals, particularly in children in the first years of life, in convalescents following wasting disease or after protracted undernutrition.

During fever abnormal amounts of protein are broken down and in protracted febrile illness, particularly if it be complicated by anorexia, large quantities of body protein may be lost, (by preference that of the skeletal muscles).

A similar increase in protein breakdown takes place in many diseases which lead to "cachexia" (leukæmia, tuberculosis, and many cases of carcinoma).

The nitrogen derived from the breakdown of protein is, for the most part, excreted in the urine and principally as urea; a smaller proportion leaves the body in the stool. The amount of nitrogen in the stool amounts, upon a liberal diet, to about 1 gm., and during fasting, 0.2 gm. per day. If the total urinary nitrogen per 24 hours be determined analytically, and to this value be added the 0.2–1.5 gm. presumably excreted in the stools, one obtains an estimate of the rate of protein breakdown in the body. Each gram of nitrogen in the urine and stools represents the breakdown of 6.25 gm. of protein or 29.4 gm. of muscle (1 gm. of nitrogen represents 2.9 gm. of protein and 13.7 gm. of muscle).

If the protein content of the food be known and if it be determined how much is lost in the stools, it is possible, by comparing these figures with the nitrogen excretion in the urine, to draw conclusions as to whether the organism is maintained in nitrogen equilibrium by such a diet or whether protein is lost or stored. If, for example, a patient with typhoid fever ingest 5.977 gm. N in the diet for 24 hours, if, further, 1.087 gm. is lost in the stools, and if, finally, 19.488 gm. N be excreted in the urine, his body has in this time excreted 14.59 gm. N more than it has taken up, i.e., he has lost 91.2 gm. protein (14.59×6.25) or 429 gm. muscle (14.59×29.4) from his body.

No accurate comparison of the urea excretion of patients with that of normal individuals under entirely different conditions of nutrition is possible. With disease of the urinary organs, particularly with certain types of renal disease, e.g., contracted kidney, all of the end products of protein metabolism cannot be excreted in the urine but are retained in the body where they accumulate as "non-protein nitrogen" in the blood and various organs (see page 146). Since these materials are, in a way, poisonous to the organism their retention is accompanied by symptoms of intoxication which are known together as **uræmia**, (headache, vomiting, cachexia, hyperirritability, mental confusion, muscular twitchings, drowsiness, clouding of consciousness, and finally coma, or,

more rarely, convulsions). Uræmic symptoms of a somewhat different nature (headache, severe epileptiform generalized tonic-clonic convulsions with loss of consciousness) develop in the course of certain renal diseases which are not associated with a disturbance of nitrogen excretion nor with an elevation of the blood non-protein nitrogen, i.e., certain forms of acute nephritis with œdema.

Among the nitrogen-containing constituents of the body the **nucleins** or nuclear substances are particularly significant. They form the principal constituent of the cell nucleus, and are correspondingly present in all organs, and animal tissues which are utilized as food, e.g., in muscle, and, in particularly large quantities, in the more cellular organs, e.g., thymus, pancreas, liver, and spleen. Breakdown of the nucleins results in the formation of protein, phosphoric acid, sugar, and as characteristic products, the nuclein-bases (hypoxanthine, guanine, and adenine). As the nucleins are broken down and transformed in metabolism, oxidation of these nuclein bases leads to the formation of hypoxanthine and xanthine and finally, by further oxidation, uric acid (trioxypurin, see page 188). Uric acid is not formed in the human body from substances other than nuclein-bases; in particular, proteins in general are not broken down in the human metabolism to uric acid but to urea. During fasting, as well as upon diet containing no nuclein, i.e., "purin-free diet" a certain quantity of uric acid continues to be excreted in the urine; this arises from the nuclear substances of the body itself and one must, therefore, assume that, in the cells and cell nuclei in the organisms, a continual rebuilding is taking place. The amount of this "endogenous" uric acid varies in different individuals but is relatively constant in any one person; it amounts in the normal adult man to 0.2–0.6 gm. per day. If the diet contain large amounts of nuclear substances, e.g., a meat diet, the uric acid excretion increases. As a matter of fact, however, the uric acid in the urine does not represent the total amount of nuclein in the food but considerably less since, in the intestine, a portion of the nuclein in the food is broken down and is not absorbed as such, i.e., only about 1/3 of the ingested nuclein material is to be accounted for in the urine as uric acid. This uric acid, arising from the

Content of common foodstuffs in nuclein bases (calculated as uric acid[1]).

Extract of meat	2–5%
Sweet bread	0.99 –1.2 %
Liver	0.3%
Beef	0.1 –0.18 %
Fowl	0.185%
Pork	0.146%
Veal	0.114–0.19 %
Mutton	0.08 –0.186%
Fish	0.1 –0.2 %
Beans	0.077%
Lentils	0.078%
Oatmeal	0.064%
Peaflour	0.047%
Black bread	0.040%
Bouillon	0.03 %
Beer	0.016%

metabolism of nuclein in the food, is spoken of as "exogenous uric acid." It varies somewhat with the nuclein content of the food but averages 0.2–0.6 gm., and this, added to the endogenous uric acid, brings the total uric acid output to 0.4–1.2 gm. per day. Uric acid is the **end product** of the nuclein metabolism and, in the human being, is not further broken down, e.g., into allantoin or urea.

The nuclein-rich foods, including not only meat and sweetbreads but also bouillon and meat extract, should be restricted in the diet of any case of gout; it is also necessary, in such cases, to eliminate the intake of wine and beer or to reduce it to a minimum since these alcoholic beverages, while they contain no nuclein substances, very commonly call forth attacks. White bread, rice, tapioca, noodles, macaroni, milk, cheese, and eggs contain so little nuclein bases that they are practically "purin-free." The methylated purin derivatives, i.e., caffein (trimethylxanthine), theobromin and theophyllin (dimethylxanthine) are not transformed in the organism into uric acid and it is, therefore, not necessary to eliminate them from the diet in gout. Chocolate, cocoa, roasted coffee and tea contain about 1.3–3% purin substances.

The daily excretion of uric acid in chronic **gout** is sometimes strikingly lowered (0.1–0.2 gm.), and it is characteristic of gout that, after a purin-rich diet, or following the

[1] Since uric acid contains 33% nitrogen the purin nitrogen may be calculated by dividing the above values by 3.

administration of nucleic acid salts or the injection of sodium urate, the uric acid excretion increases less rapidly than in the normal individual. The uric acid excretion just preceding an **acute attack of gout** is sometimes diminished while, during the attack, and for a short time immediately following, it is sometimes increased. Gouty patients usually show an increase in the uric acid of the blood, particularly if they have been confined to a purin-free diet for a day or two before the blood is taken for examination. In the normal, the uric acid content of the blood is from 2 to at most 3.5 mg. per 100 c.c., in gout commonly 4–9 mg. or above. An elevation of the uric acid content of the blood occurs not only in gout but sometimes, and to a more striking degree (6–12 mg.), in renal disease or in leukæmia. For the methods of determination of the uric acid in blood and urine see pages 137 and 148.

The **nitrogen-free** foodstuffs, i.e., the **carbohydrates** and **fats** (as well as the nitrogen-free substances, e.g., glucose, formed in the intermediate protein metabolism) are oxidized in the body to carbon dioxide and water, which are eliminated principally with the expired air.

The volume of CO_2 eliminated with the expired air amounts to about 800 gm.–400 liters—per 24 hours at rest and upon the average diet; the amount of oxygen absorbed in a similar period is about 715 gm.–500 liters. At complete rest and fasting, i.e., 12–14 hours after the last meal, about 2.85 c.c. CO_2 is expired and 3.47 c.c. oxygen absorbed per kilo body weight per minute. This proportion

$$\frac{CO_2 \text{ expired}}{O_2 \text{ absorbed}} = \frac{2.85 \text{ cm.}}{3.47 \text{ cm.}} = 0.82$$

is known as the respiratory quotient and, upon a mixed diet, its value is less than 1, usually about 0.75–0.8. With excessive carbohydrate administration it approaches 1, since then approximately as much CO_2 is breathed out as oxygen is absorbed; upon a predominantly fat diet and during fasting it sinks to about 0.7. With the ingestion of food, and particularly upon a high protein diet, the metabolism is generally raised and therewith the CO_2 production and the oxygen consumption are increased by about 10%.

The elimination of water via the lungs and through the skin (perspiration) amounts at rest and room temperature to from 500 c.c. to 1 liter per 24 hours; with exercise and in the open air to 1.5–2.5 liters and with violent exercise, e.g. mountain climbing, it may amount to 3–5 liters. The evaporation of 1 liter of perspiration frees from the skin about 580 calories.

If it is desired to bring about an improvement in the nutrition of a patient or an increase in the body weight, it is necessary to administer, in addition to large amounts of protein, considerable quantities of nitrogen-free food stuffs. Since fats cannot be well tolerated in larger quantities than 150 gm. it is important to raise the carbohydrate intake as much as is reasonably possible. At the same time rest is advantageous. If, on the other hand, it seems advisable to bring about a reduction in weight (with obesity) it is necessary to administer only adequate amounts of protein and to reduce the intake of fat and carbohydrates (bread, potatoes, pastries and sugar) and to advise adequate amounts of exercise or work to bring about combustion of the body fat.

In order to determine whether a given diet is adequate for the maintenance or improvement of nutrition, or, further, to calculate whether protein is lost or stored in the organism, it is often necessary to know the composition and the caloric value of the various food stuffs. The more important figures are summarized in the table on pages 506–507.

In **diabetes mellitus** the organism has lost to a varying degree its ability to burn and to utilize carbohydrates; glucose accumulates in the blood and is excreted in the urine. In place of this, the body metabolizes large quantities of protein and fat. Since, in the normal state of nutrition, over half the caloric demands of the body are satisfied by the carbohydrate in the food and since, in diabetes, this phase of metabolism is seriously impaired, considerable quantities of the body fat and protein are metabolized, leading often to pronounced loss of weight. Some diabetics may continue to excrete sugar upon a carbohydrate-free diet, for the reason that some of the body protein is transformed into sugar. This production of sugar from protein may be so extensive that it is necessary to reduce the protein intake, particularly that of eggs and meat.

In the most severe cases of diabetes all the sugar is voided

FOOD	Protein %	N %	Fat %	Carbohydrate %	Cal. per 100 gm.
Raw beef, lean	21.9	3.4	0.9	....	84
Raw beef, medium fat	18.4	2.9	5.2	....	136
Raw beef, fat	16.9	2.7	27.2	....	322
Boiled beef (100 gm. raw, cooked to 57 gm.)	36.4	5.8	8.8	....	231
Roast beef (100 gm. raw = 80 gm. roast)	25–30	4.9	7.5	....	195
Raw veal	15.3	2.4	1.3	....	75
Roast veal (100 gm. raw = 78 gm. roast)	28.4	4.5	1.3	....	128
Pork chop	35.0	4.5	10.0	....	236
Boiled ham	24.0	3.8	36.7	....	439
Smoked tongue (ox)	35.2	5.6	45.8	....	570
Bacon	9.5	1.5	76.4	....	749
Sausage	20.7	3.3	53.1	....	578
Venison	28.2	4.5	5.5	....	149
Broiled young chicken	32.1	5.1	4.4	....	181
Shell fish	24.3	3.9	0.5	....	104
Herring	19.0	3.0	7.1	....	144
Hen's eggs (without shell)	14.1	2.2	10.9	....	159
1 Egg (about 45 gm.)	6.3 gm.	1.0 gm.	4.9 gm.	....	71
Cow's milk	3.4	0.5	3.6	4.8	67
Cream	3.7	0.6	25.0	3.5	268
Butter	1.0	0.1	82.8	....	774
Swiss cheese	27.2	4.3	30.4	2.5	404
Wheat flour	11.0	1.8	1.3	74.2	360
Wheat bread (rolls)	8.1	1.1		62.7	290
1 Roll = 50 gm.	4.0 gm.	0.6 gm.		31.3 gm.	145
Black bread	6.2	1.0	0.2	51.2 gm.	238
Raw or boiled potato	1.8	0.3	0.2	20.6	93
Raw dried peas	22.8	3.6	1.8	52.4	325
Rice	7.5	1.2		78.1	351
Meat broth		0.06	0.8	....	7
Rice soup	0.5	0.08	0.8	3.2	22
Pea soup	4.0	0.6	0.3	8.8	55
Rice and milk	5.9	0.9	9.1	29.4	358
Purée of potato	3.2	0.5	6.5	20.7	158
Spinach (cooked with butter)	3.8	0.6	8.0	8.0	122
Sauerkraut (" " ")	1.7	0.3	23.0	5.0	241
White wine	....	....	....	0.4	83
Red wine	....	....	....	0.6	70
Sherry	0.2	0.03	....	3.3	136
Beer	0.8	0.1	....	4.1	45
Café au lait	0.8	0.1	0.9	1.2	16

More common alcoholic beverages contain:

Beer	3.6–4.0%	alcohol[1]
Bordeaux wine	8 %	"
Rhine wine	7–10%	"
Malaga	16 %	"
Champagne	10 %	"
Brandy	45 %	"
Cognac	50–60%	"

in the urine which could be derived from protein; since protein metabolism may be calculated from the nitrogen content of the urine, the proportion of urinary nitrogen to urinary sugar gives a useful measure of the degree of protein breakdown and sugar formation. The relation of the dextrose (D) to the nitrogen (N) in the urine may in the severest cases of diabetes amount to 3.65 gm. D to 1.0 gm. N, from which it may be calculated that from 6.25 gm. protein (1 gm. nitrogen) 3.7 gm. glucose (58%) may be formed.

In diabetes mellitus the blood sugar is conspicuously raised, up to 200 or even 500 mg. %, as contrasted with the normal value (fasting) of 80–120 mg. %. For the methods of the determination of the blood sugar see page 149.

The therapy of diabetes mellitus should be directed toward the reduction of the blood sugar, the elimination of glycosuria, the improvement of nutrition. This may in some cases be accomplished by reduction or withdrawal of the diet carbohydrate and the administration of sufficient carbohydrate-free foods (all sorts of meat, fish, eggs, cheese; large quantities of fat, butter, bacon, and carbohydrate-free green vegetables). Sugar and sweet foods and drink must be eliminated first. A diet totally devoid of carbohydrate can be tolerated only with difficulty; the administration of small amounts of carbohydrate is unavoidable. In mild cases it is possible to allow the patient as much carbohydrate as can be taken without causing the appearance of sugar in the urine. This "carbohydrate tolerance" may be determined by adding to a weighed and measured diet about 30 gm. of carbohydrate daily until the urinary sugar reaction becomes positive. An amount of carbohydrate somewhat smaller than this may then be administered daily; if for example, upon the addition of 100 gm. carbohydrate a trace of sugar appears in the urine

[1] 1 gm. alcohol produces 7.2 calories.

one prescribes 60–80 gm. The carbohydrate contents of various foods are summarized in the following table.

Carbohydrate Equivalent of 100 gm. White Bread

60 gm.	Sugar.
70 gm.	Zwieback, cake, pastry without frosting.
80 gm.	Wheat, rye, or oat flour, rice, barley, sago, noodles, macaroni, grits.
100 gm.	Brown or oat bread, biscuit.
120 gm.	Rye, gluten or graham bread, pumpernickel, dried peas.
150 gm.	Aleuron bread, D K bread or fruit cake without sugar.
300 gm.	Cocoa, chestnuts or grapes, potatoes.
500 gm.	Fresh peas or beans.
600 gm.	Beets, apples, pears, cherries, prunes, apricots, peaches, raspberries, gooseberries, pineapples, walnuts, hazelnuts.
800 gm.	Strawberries, whortleberries, almonds, melons.
1000 gm.	Oranges.
1250 c.c.	Milk.
1500 c.c.	Cream.
1500 c.c.	Dark beer.
2000 c.c.	Light beer.
2500 c.c.	Kephir.

If it is not possible to reduce the sugar content of the blood and to cause sugar to disappear from the urine by dietary measures alone, or if a positive reaction for acetone or diacetic acid appear in the urine (see page 220), the danger of acidosis makes necessary the administration of insulin. This substance, prepared from the pancreas of animals, is administered subcutaneously in divided doses two to three times a day. If insulin be used in too large amounts the blood sugar may be so reduced that the symptoms of hypoglycæmia appear (tremor, perspiration, weakness or occasionally convulsions). These symptoms may be almost immediately relieved by the administration of 40–50 gm. sugar.

(In practice it is advisable to determine the metabolic requirements of the individual and to meet them by a diet containing 0.7–1.0 gm. protein per kilo (ideal weight) with carbohydrate and fat sufficient to furnish the remaining calories, and in such proportion that the available fatty acid is to available glucose as 1.5 : 1. The urine should be collected in total specimens from before one meal to before the next; insulin is gauged according to the glycosuria, 1 unit per 1.5–2.0 gm. urinary sugar. Thus, if the afternoon specimen contain 10 gm. glucose the patient should receive 5 units insulin 20 minutes before lunch. Ed.)

The food substances are not completely absorbed in the intestinal canal; a certain proportion is always evacuated with the stool. Under normal conditions animal protein (meat, egg, cheese, etc.) is almost completely utilized while plant protein (black bread, beans and peas) is less well absorbed; from certain forms of bread (made of white flour, rice, etc.) the protein may be utilized almost as well as that of meat or eggs. Carbohydrate (starch and sugar) is usually almost completely absorbed, but of the fat, on the other hand, a larger proportion is unused and passed with the stool. Under certain pathological conditions the utilization of food is less complete than in the normal, e.g., with severe diarrhœa. In the absence of bile in the intestine (obstructive jaundice) the absorption of fat is seriously impaired; with complete obstruction of the gall-duct three-fourths of the ingested fat passes out in the stool. In many severe affections of the pancreas the absorption of fat as well as that of protein is very much reduced.

Finally there are several proportions which are often necessary in metabolic calculations:

Nitrogen : urea	—1 : 2.14
Nitrogen : protein	—1 : 6.25
Nitrogen : meat	—1 : 29.4
Urea : nitrogen	—1 : 0.466
Urea : protein	—1 : 2.9
Urea : meat	—1 : 13.7
Protein : nitrogen	—1 : 0.16

Certain Data Concerning the Development and Nutrition of the Child

The height and weight of the normal full-term infant change as indicated in the table on page 510.

The body weight falls during the first three days of life by about 200 gm. (6½ oz.). Thereafter there is a daily gain of 15–16 gm. (½ oz.) during the first six months, 10–15 gm. (1/3 oz.) during the second, and after the first year 3–10 gm. The body weight has doubled at the end of the first five months, and trebled at the end of the first year.

Skeleton. The temporal and occipital fontanelles close soon after birth but the large frontal fontanelle remains open for 12–16 months. In normal individuals the scalp over the fontanelle is somewhat tense and rises and falls with respira-

Age	Body Length				Body Weight			
	Boys		Girls		Boys		Girls	
	cm.	in.	cm.	in.	kg.	lbs.	kg.	lbs.
1 day	50	20	50	20	3.2	7	3.2	7
3 days	50	20	50	20	3.0	6½	3.0	6½
2 weeks	51	20½	51	20½	3.7	8	3.7	8
1 month	53	21	53	21	4.4	9½	4.4	9½
2 months	55	22	55	22	5.0	11	5.0	11
3 "	57	23	57	23	5.6	12¼	5.6	12¼
5 "	60	24	60	24	6.4	14	6.4	14
8 "	65	26	64	25½	7.5	16½	7.4	16¼
10 "	67	27	67	27	8.2	18	8.2	18
12 "	70	28	70	28	9.0	19¾	9.0	19¾
2 years	80	32	80	32	11.5	25½	11.5	25¼
4 "	96	38½	95	38	15.5	34	15.3	33½
5 "	103	41	102	41	17.5	38½	17.0	37½
6 "	109	43½	108	43	19.0	41¾	18.5	40¾
7 "	115	46	114	45	21.0	46¼	20.0	44
8 "	120	48	120	48	22.5	49½	22.0	48½
9 "	125	50	125	50	25.0	55	24.0	52¾
10 "	130	52	130	52	27.0	59½	27.0	59½
11 "	135	54	134	53½	30.0	66	29.0	63¾
12 "	140	56	139	55½	32.0	70½	32.0	70½
13 "	144	57½	145	58	35.0	77	36.0	79¼
14 "	148	59	150	60	38.0	83½	40.0	88
15 "	156	62½	154	61½	45.0	99	45.0	99

tion and with the pulse beat. With desiccation, cardiac failure, or collapse, the fontanelle is lax and sunken. With any increase in intracranial pressure, e.g., transudative or exudative increase in the spinal fluid, hydrocephalus, meningitis, it is tense and bulging.

The eruption of the milk teeth begins in the 5th to the 8th month of life and is complete by the 24th–30th month (20 milk teeth). The order of eruption of these teeth is described on page 248. The change of teeth begins in the 5th–7th year of life.

Physical and psychological development. 1st month: Impulsive reflexes and instinctive movements (e.g., swallowing, sneezing, yawning, sucking), auditory function and coordinate movement of the eyes. **2nd month:** Child begins to

babble and is first able to raise the head. **3rd month:** Fixes the eyes on objects which are for the first time recognized, hearing develops further, smiling. **4–6 months:** Grasps, sits up, holds up the head. **3rd quarter:** Begins to speak syllables, stands with assistance. **4th quarter:** Walks with assistance. **5th and 6th quarters:** Stands and walks alone, may speak several words. **7th and 8th quarters:** Speaks sentences.

Nutrition: The sole natural nourishment and, at the same time, that which is best tolerated during the first year of life, is woman's milk. The majority of women are able to furnish this nutrition, at least with proper care, though the onset of lactation may be somewhat delayed and the quantity of milk sometimes no more than sufficient. Certain contraindications to nursing may be raised on the part of the mother; the most important of these are pulmonary tuberculosis, streptococcus infections, wasting diseases, epilepsy or psychosis. The presence of active syphilis in mother or child is no contraindication since the transmission of this disease in either direction is practically unknown. The contrary is true in the case of a nurse with syphilis. Nursing on the part of the mother may be interfered with by abscess of the breast or inflammation or anomaly of the nipples (in this case the child should be put to the breast for a short time in order to prevent too great stasis in the gland). On the part of the child, cleft palate, inefficient sucking, or unconsciousness make nursing impossible. The child is first nursed on the 2nd day of life and thereafter, every three to four hours during the day and not more than once at night; in the presence of scanty secretion, at both breasts, otherwise alternately at the right and the left. The daily requirement of a nursing child increases during the first week of life up to 1/6 to 1/5 his body weight and falls during the 2nd quarter to 1/7 or 1/8 thereof. If the mother's milk be insufficient supplementary feeding is necessary. Weaning should be accomplished gradually, usually about the 6th month, and, if possible, not during the warmer season.

Artificial feeding of infants should be undertaken only when human milk is unavailable. This practice leaves much to be desired in regard to the tolerance and resistance of the child, particularly in the face of nutritional difficulties. For artificial feeding the fresh, clean milk of healthy cows serves

best. Undiluted, such milk is not well borne by young infants and is, therefore, best diluted with water. Obviously the nutritional value of such a dilution is less than that of human milk; in order to supply the nutritional demands of the child, without increasing too much the daily volume, a certain number of calories must be added. This is best accomplished by the addition of carbohydrate rather than fat. The total daily **milk** feeding should not amount to over 1/10 the weight of the child at that time. This quantity should correspond to about 70 calories per kilo. Since the daily requirement of the infant during the first quarter is at least 100 calories per kilo 40 calories per kilo (10 gm.) carbohydrate must be added. In other words, the child should receive 1/10 the body weight of cow's milk and 1/100 the body weight as carbohydrates; this mixture is diluted up to ¾ to 1 liter with water, the total is divided into 5 or 6 portions, and feedings are given at intervals of 3–4 hours during the day, with an 8-hour pause at night.

During the first 4 weeks carbohydrate may be given in the form of sugar (cane sugar or lactose) or gruel (a 4% mixture of barley, oatmeal or rice boiled with water and strained) and from 4 months on as oatmeal. The customary formula for artificial nourishment of infants rests upon an empirical basis; an attempt to approximate the artificial feeding to the natural as regards its gross chemical make-up often defeats its purpose. The fact that bottle feeding is less efficient than the natural is not due to differences in protein, fat and carbohydrate content of the animal milk but to species difference, an observation which may be repeatedly made in an attempt to nourish new-born animals of various species.

The artificial feedings are best sterilized by heat (water bath) in single portions. Most rigid precautions in the preparation and cooling of the food are to be observed in the summer. On the other hand, the milk should not be allowed to simmer for more than 5 or at most 10 minutes since it is thereby so altered that its use may result in faulty nutrition, e.g., rickets or Mœller-Barlow's disease.

The signs of good nutrition in the infant are the following: Normal function of the organs, normal and sequential development of motor and static functions (see above), normal

turgidity of the tissues and tension of the musculature, normal activity in the voice, temperature variations over only a few tenths of a degree, normal growth, and resistance to alimentary and bacterial disease, smooth skin and mucous membranes of normal color, normal number and quality of the stools.

From the 6th month on the healthy child may receive gruels, bread and milk, and soup (meat broth in which there is oatmeal, rice, tapioca or sago, cooked). By the 12th month at the latest and, if possible, earlier he should be fed vegetable purées and fruit juices. After the first year, egg and finely ground meat may be added.

Abnormalities of nutrition are encountered predominantly in artificially fed children. The acute disturbances are, for the most part, associated with diarrhœa and are due to the quality and composition of the food, to constitutional peculiarities or to infection either within or without the gastro-intestinal tract. These vary in form from **dyspepsia** to the most severe **diarrhœa**, known as **cholera infantum** or intoxication. The first signs are generally moderate increase in temperature, diminished food intake, pallor and restlessness, vomiting, frequent, soft, often greenish, stools. The later and more alarming symptoms are convulsions, cramps, hyperpnœa, vomiting, fluid stools, polyuria, and finally the signs of desiccation with sudden loss of weight.

The **chronic disturbances of nutrition or dystrophies** may begin with gastro-intestinal symptoms but are more obviously disturbances of metabolism: Growth suffers or ceases. These are often combined with acute processes. The most common form of dystrophy is **heterodystrophy**, i.e., occasioned by the unnatural type of feeding; the infant (at the same time perhaps suffering from rickets or eczema) shows abdominal distention, soapy, sometimes crumbly stools, vomiting, weakness, pallor and maldevelopment.

To the dystrophies belong also the **avitaminoses** which appear in malnourished infants, sometimes as scurvy or keratomalacia, sometimes in less characteristic form.

Protracted chronic disturbances of nutrition may not only lead to depletion of the body reserves and depots but may also interfere with growth. In such cases one speaks of pæda-

trophy. Rapid disappearance of body fat, an aged appearance, increased muscle tonus, grayish skin, bradycardia and hypothermia are signs of this severe condition. Proper nutrition under these circumstances may work wonders but undernutrition soon leads to collapse. The lack of resistance against bacterial infection is often suggestive: Such infants are particularly prone to infections of the stomach, lungs, skin; and these complications often lead to death.

Nursing. During the first year of life the child should be bathed daily in pure water at about 35° C. After each voiding of urine the infant should be thoroughly dried and after a stool should be carefully washed and dried. The clothing of the child should permit free movement of all the extremities. The mouth should be thoroughly rinsed following each meal. The child should not be permitted to be accustomed to a "pacifier." The nursery should be airy, sunny and clean. Access to the child or to his surroundings should be strictly denied to persons with open tuberculosis.

CHAPTER XI

DISEASES OF THE SKIN

THE following types of cutaneous eruptions are to be distinguished:

Macule (fleck); **papule; nodule** (tumor); **urtica** (wheal); **vesicle; bulla; pustule** (vesicle containing pus).

Macules or flecks are circumscribed alterations in color of the skin without any elevation. They may be caused by localized hyperæmia, in which case they are designated as **roseola** when they are small and dispersed (typhoid, syphilis, typhus), or as **erythema** when they are larger, more diffuse or confluent (scarlatina, erythema multiformi, erythema medicamentosa). Extensive hæmorrhages into the skin are known as **echymoses,** smaller hæmorrhages as **petechiæ,** and when distributed in stripes as **vibices.** The spots caused by hæmorrhage are brownish-red and are distinguished from localized hyperæmia by the fact that pressure with the finger or with a glass slide does not cause them to pale or to disappear.

Purpura rheumatica is characterized by an eruption of small intracutaneous hæmorrhages, about the size of the head of a pin, which usually appear either alone or most extensively over the lower extremities, and whose outbreak is accompanied by pain in the limbs and sometimes by swelling of the joints. In **purpura hæmorrhagica** or Werlhof's disease the hæmorrhages are distributed not only over the skin of the entire body but also upon the mucous membranes (nose, mouth, conjunctiva and intestine).

Erythema infectiosum is an uncomplicated communicable disease of childhood. It appears suddenly, usually with a butterfly reddening over the cheeks with several rings or macules at the margin. By the following day the erythema has extended to cover the upper extremities as an exanthem, at first disc-like and then rapidly becoming confluent; it spreads to the trunk and on the third or fourth day of the disease involves the legs. The exanthem fades and disappears upon

the 6th to the 8th day. Relative eosinophilia (7–9%) and lymphocytosis (35–37%).

Abnormal accumulations of pigment may produce **brown spots** (nævi, birthmark; lentigo, freckle; ephelides). The absence of pigment produces abnormal light areas (leucoplakia, vitiligo). In syphilis there may appear a spotty pigment atrophy about the neck (leucoderma syphiliticum). In cases infested with pediculis pubis bluish flecks are often observed over the chest and abdomen (maculæ cœruleæ).

Papules, nodules are circumscribed elevations above the level of the surrounding skin due either to an inflammatory or non-inflammatory accumulation of cells. In the first case the papule is red (hyperæmia).

Lichen consists of small nodules which do not undergo further transformation (to vesicles or pustules). The following types are distinguished: Lichen pilaris (keratosis pilaris), small, firm, symptomless nodules which are suggestive of goose-flesh and are produced by the accumulation of cells of the horny layer of the epidermis about the opening of the hair follicles; they are usually found upon the extensor surface of the arm and thigh. **Lichen scrophulosorum** (tuberculosis lichenoides): Minute yellowish-brown papules usually arranged in groups or circles over the trunk of scrophulus, i.e., tuberculous, individuals. In the strict sense only lichen ruber is to be considered as lichen; of this there are two chief forms. **Lichen ruber planus:** Purplish-red, firm, flat, polygonal, waxy nodules which sometimes itch, and involve particularly the flexor surfaces of the extremities. Here they are arranged in groups or rows and where they are particularly abundant lend to the skin an appearance of grain leather. Upon the mucous membrane of the mouth and tongue they are often morphologically altered. About the genitalia lichen may be easily confused with syphilitic lesions. The rare **lichen ruber acuminatus** is distinguished from the other form in that the nodules are pointed and bear scales upon their points. The affected areas of the skin are stiff and, in the folds, may be painfully cracked. Lichen ruber is a chronic disease.

Tumors. In this group belong the neoplasms (carcinoma and sarcoma) lepra tuberosa, rhinophyma, and erythema nodosum. The latter appears particularly upon the arms and

lower legs, as painful, bluish-red nodules the size of a walnut; it heals within 1–2 weeks and undergoes all the color changes characteristic of the resorption of hæmorrhage following contusion.

Urtica or **wheal** is a term given to a circumscribed, flat, red or pale elevation of the skin which arises rapidly and quickly disappears. In contrast with papular lesions these are not occasioned by an accumulation of cells but by a localized exudation of fluid into the skin. In addition to wheals of moderate size which appear as urticaria or nettle rash and cause terrific itching and burning, diffuse, large, infiltrated areas sometimes appear in the skin due to nervous or vaso-motor disturbances (**angioneurotic œdema**). Also small, dispersed, firm, itching nodules which are apparently urticarial in nature, appear in **scrophulus infantum.** True papules sometimes widely distributed, are known as **prurigo** and are probably closely related to urticaria. In **prurigo hebiæ,** a rare and incurable condition beginning in childhood, the affected areas, particularly the extensor surfaces of the extremities, are densely infiltrated and the regional lymph glands are swollen.

Vesicles or **blisters:** Due to a serous exudation beneath it the uppermost layer of the epidermis is raised from the underlying cells. The contents, at first water-clear and later usually cloudy, shimmer through the top of the vesicle which is usually of a pin-head size or slightly larger. These lesions appear in all types of dermatitis, particularly in eczema, which to many authors is synonymous with dermatitis, and above all, in those chronic and relapsing inflammations of the skin which appear to be due to some endogenous constitutional factor. Dermatitis and eczema represent inflammations of the skin which are analagous to catarrh of the mucous membranes; they may arise from the most varied internal and external causes. In the less severe acute, and the majority of the chronic forms there occurs not only vesicle formation followed by the exudation of fluid and formation of crusts, but also an eruption of minute papules. The skin is reddened, often thickened, and, in acute cases, sometimes œdematous, particularly about the face, backs of the hands and genitalia.

Miliaria crystallina is characterized by the formation of small pin-head-sized, clear vesicles which cover the skin of the trunk like drops of dew. These are caused by the retention of perspiration and appear chiefly with febrile diseases after profuse sweats; they are without significance.

Vesicles which form in groups upon a reddened and inflamed base are characteristic of **herpes** (herpes labialis and facialis with febrile diseases, e.g., pneumonia and meningitis). **Herpes zoster** or "shingles" is characterized by an eruption of vesicles the distribution of which corresponds to a sensory segment of the cord or to a single branch of the trigeminus. It is due to inflammatory stimulation of an intervertebral ganglion or the Gasserian ganglion. Herpes progenitalis is the term applied to a vesicular eruption upon the external genitalia, particularly upon the inner surface of the foreskin; it in no way represents a venereal disease, it heals rapidly but is prone to recur.

Bullæ, or pemphigus vesicles are large vesicles which occur with fulminant dermatitis, e.g., erysipelas, following burns, freezing, and diabetic gangrene and in addition with various nervous diseases, syringomyelia, and leprous and traumatic disease of the peripheral nerves; finally they are a common accompaniment of true pemphigus.

Pemphigus neonatorum occurs in new-born infants as a communicable and relatively harmless infectious disease usually caused by streptococci or staphylococci. The **pemphigus chronicus** of adults is a severe and chronic disease, not infrequently fatal, in which vesicles occur in repeated crops over the entire surface of the skin and upon the mucous membrane of the mouth, pharynx, nose and eyes. Occasionally it is accompanied less by the formation of vesicles than by the extensive exfoliation of the skin in whole sheets (pemphigus foliaceus). **Dermatitis herpetiformis** (Duhring) is a benign but often relapsing form of pemphigus accompanied by violent itching, in which the vesicles usually remain small and occur in groups similar to herpes; usually other types of efflorescence (erythema, papules or wheals) are also present.

Pustules are a form of vesicle filled with pus and surrounded by an inflamed, reddened zone. To this group belong

the lesions of variola, some of the rarer syphilitic lesions and finally **acne.** This latter is caused by inflammation and pus formation in the hair follicles usually as a result of stasis of the secretion in the glands. Its points of predeliction are the face, chest and back. Acne may also result following the internal administration of bromine or iodine. While in the acne pustule there is actually cell infiltration, in the center of which pus formation takes place relatively late, in the more common folliculitis superficial pustules appear early, associated with a secondarily inflamed and œdematous area in the neighborhood. This form of folliculitis, which as a rule is caused by staphylococci, belongs, together with the non-follicular impetigo contagiosa (usually caused by streptococci), and with the related pemphigus neonatorum, in the large group of **pyodermia.** If an inflammatory process in the hair follicles penetrate into the deeper layers and lead to necrosis it is spoken of as a **furuncle.**

The following are designated as **secondary skin changes: scales; crusts; erosions,** defects of the epidermis only, do not bleed; **excoriations,** the defect penetrates into the cutis and bleeds; **ulcers; scars.**

Scales result from the heaping up and exfoliation of dead and dried epidermis. According to the size of the desquamated sheet of skin, exfoliations are distinguished as branny or lamellar. Upon the mucous membranes, e.g., that of the mouth, cornification rarely takes place; the epithelium remains in place and forms white, moist plaques e.g., the mucous patches of secondary syphilis. In some pathological conditions, however, true cornification occurs.

Among the scaling or squamous exanthemata belong, in addition to some forms of eczema, the following: **Eczema seborrhoicum** which causes the formation of scales upon the scalp and often leads to baldness; **Ichthyosis,** a congenital anomaly in which the horny layers of the skin are particularly tenacious and brittle; **pityriasis versicolor;** yellowish-brown, scaly flecks on chest and back (do not itch) in the epidermal layers of which microsporon furfur is demonstrable (see page 304); **psoriasis,** a benign but chronic and relapsing abnormality, is characterized by the appearance of brownish-red flecks which form a sheet of glistening scales. By virtue

of the peripheral growth and confluence of this efflorescence there may form a ring covered by asbestos-like scales; the point of predeliction of this process is the folds of the knees and elbows but it may also appear upon the chest, back or scalp.

Crusts are due to the drying of exudate upon the skin; they appear as yellowish, transparent masses when they are due to the drying of serous fluid or opaque, yellow or brownish when they are brought about by the drying of pus, or blood. These crusts are round and circumscribed if they are preceded by vesicles or large and irregular in shape when they result from a more diffuse outpouring of fluid. Secondary infection with staphylococcus or streptococcus may lead to crust formation in any type of dermatosis.

Impetigo contagiosa is an infectious disease usually due to streptococcus or more rarely to staphylococcus and occurring predominantly in childhood. On the face, arms and legs as well as on the trunk, there form vesicles of a few mm. diameter which soon break; their contents are poured out upon the skin and, drying, form thick, yellowish crusts. With suitable treatment the lesions heal in from 8–14 days.

Erosions or excoriations involve loss of substance of the skin, either of the superficial layers alone or of the cutis proper; they may be occasioned by the bursting of vesicles, or pustules, or by trauma. **Rhagades** is the term given to the cracks in the skin which correspond to the normal furrows and are usually due to the stretching and tearing of the skin which has become friable (about the corners of the mouth, nose and upper lip, in the folds of the hands, particularly in chronic eczema, and arranged radially about the mouth in congenital lues).

Ulcers are penetrating, necrotic areas involving loss of substance in the skin and destroying not only the layers of the epidermis but the papillary bodies as well. Restitution, which takes place with any lesion of the epidermis alone, is not possible in the case of ulcers, these heal only with the formation of scar tissue. Cutaneous ulcers appear with lues and tuberculosis, carcinoma, and deep burns, e.g., with X-ray (extraordinarily hard to heal), on the lower legs with varices, with small-pox, about the genitalia with soft chancre,

and in a portion of the area occupied by the primary syphilitic lesions.

Scars are covered by epithelium but the true structure of the upper layers of the skin, the hair follicles, and glands are for the most part replaced by new-formed connective tissue. Scars, therefore, do not show the normal skin marking and are smooth, free of hair or pigment.

In addition to ulcers of the skin, lupus in its various forms (lupus vulgaris and lupus erythematosis) leads to the scar formation. The relation of lupus to tuberculosis is not yet established with certainty. In lupus erythematosis there forms first, frequently on the nose, a small erythematous area in the center of which are scales covering the mouth of the follicles; this area gradually spreads in a butterfly shape over the cheeks and the remainder of the face. While the process at the periphera is extending that in the center heals forming a thin, smooth scar containing dilated vessels. The cartilage of the nose and of the ears may atrophy as a result of the contraction of the scar, and the lips and eyelids may be shortened.

In **scleroderma** there form, in the absence of any preceding ulcerative process, circumscribed or diffuse scar-like changes leading to shrinking of the skin which is sometimes closely adherent to the subcutaneous tissues. The skin is wax-like, white or yellow; that about the neck and chest is most frequently involved. Eczema psoriasis and the other superficial affections of the skin, if uncomplicated, never lead to scar formation; the opposite is, however, true of acne.

The following properties of any efflorescence should be described:

Consistency. The lupus nodule is soft, often broken down, or breaks upon the slightest pressure; the syphilitic papule is firm,infiltrated, and usually tender to pressure; the nodules of lichen ruber, and of prurigo, the vesicles of varicella, and particularly those of variola, are firm; the edge of the typical primary syphilitic lesion is hard, and hardest of all is carcinoma.

Color. Erythema, as well as acute eczema, is usually bright red. Teliangiectases (persistent dilatation of the small skin vessels) are usually wine color; lichen ruber is pale red

with a bluish opaque sheen; syphilitic efflorescences are a brownish or ham-red in color; the nodules of lupus vulgaris are yellowish-brown like droplets of dark yellow wax. The small crusts of favus are sulphur-yellow; this is caused by a form of hyphomycetes, achorion Schœnleinii. Favus appears principally on the scalp, more rarely upon other areas of the body, and leads to the formation of hairless scars.

Distribution, localization, and arrangement. Some exanthemata are distributed diffusely over the entire body (scarlatina, universal eczema, dissementated psoriasis), others are limited to smaller areas of the skin. They frequently show certain areas of predilection as described above. Certain efflorescences, due to the fact that they extend peripherally while healing in the center of the lesion, form rings, the confluence of which may lead to serpentine figures. This is frequently observed in the skin diseases due to parasites, e.g., trichophytia superficialis (herpes tonsurans), which forms rings with flat, scaly or, more rarely, vesiculated borders, and is caused by trichophyton tonsurans (see page 303). If this organism grow in the region of the beard or the scalp the ring-form of the lesion is less apparent, in these areas the hair rapidly falls out. Certain other skin diseases, the parasitic nature of which is not yet certainly established, also form these rings: Psoriasis, eczema, urticaria; and erythema multiforme. In the latter there appear, upon symmetrical areas of the extensor surfaces of the hand and forearm, or more rarely upon the face, feet and trunk, red spots which, in the course of a few days, form circles with bluish-red or bullous centers. This disease occurs principally in the spring or the autumn, usually appears in young people; it is accompanied by a sensation of heat in the lesions or more rarely by mild itching; it heals after a few days.

In the case of a diffuse exanthem it is important to differentiate whether the lesions are everywhere the same or are polymorphous. The latter is an important diagnostic sign of the syphilitic exanthem in which macules, urticarial macules, small and large papules, vesicles, pustules or even ulcers, may appear at the same time. In purpura rheumatica, mentioned above, petichiæ sometimes occur associated with erythematous, urticarial and papular lesions.

The most important subjective symptom of cutaneous disease is **itching.** Two forms of itching may be distinguished, one which seems to demand rubbing, e.g., urticaria, and another demanding energetic scratching, e.g., prurigo and pediculi vestimentorum. Itching exanthemata of the latter type often show bloody excoriations caused by the finger nails. Severe itching (pruritus) may also arise in the absence of cutaneous disease, as with jaundice, nephritis, diabetes, in elderly people (pruritus senilis), with varices of the lower leg, hæmorrhoids, etc. While some skin lesions, e.g., the syphilitic, are distinguished by the absence of itching, in other forms it is usually present, e.g., eczema, urticaria, lichen ruber and worst of all with prurigo. Infestation with animal parasites is often accompanied by terrific itching, e.g., lice, etc.

The lesions of **scabies** occur principally about the joints of the hand, between the fingers, in the folds of the axilla and about the umbilicus and nates. Particularly significant is their location upon the lateral side of the fingers and in the interdigital folds. The head and neck are usually unaffected. Scabies may be recognized by the demonstration of the burrow formed by the acarus scabiei in the epidermis. If this be opened with a needle the mite may be discovered at the end thereof as a small dark point. If the mite itself is not found the eggs may sometimes be demonstrated. If scabies be present for a long time it is often complicated with eczema and pyodermia (impetigo, folliculitis, furuncles).

APPENDIX

ACUTE INTOXICATIONS

INORGANIC POISONS

Poison	Symptoms	Therapy
Carbon Monoxide and illuminating gas	Dizziness, headache, nausea, vomiting, flashes of light before the eyes, dilated, fixed pupils, tinnitus, muscular weakness or paralyses, cyanosis, or bright red color of the skin, loss of consciousness, asphyxia, drowsiness, convulsions, glycosuria and albuminuria; carbon-monoxide hæmoglobin in the blood (see page 134). Sequelæ: cutaneous eruption, paralysis of the bladder and rectum, decubitus ulcers, neuroses and psychoses.	Fresh air, oxygen inhalation, artificial respiration, saline infusion. Inhalation of CO_2 5% in oxygen.
Nitrous oxide	Severe dyspnœa, asphyxia, pulmonary hæmorrhage, pulmonary œdema, exhaustion, cyanosis, pain in the chest.	Bed rest, abundant fluids, oxygen inhalation, venesection, hot packs, saline infusion.
Chlorine (a) chlorine gas	Violent coughing, sneezing, shortness of breath, outpouring of mucus from the mouth, nose and eyes, collapse, cyanosis.	Fresh air, steam inhalation venesection, sometimes tracheotomy.
(b) chlorine water	Irritation of the mucous membrane of mouth and pharynx, vomiting of material smelling of chlorine.	Dilute aqueous solution of sodium hyposulphite by mouth, albumin-containing drinks: milk and egg albumin; gastric lavage.
(c) potassium chlorate	Vomiting, diarrhœa, dyspnœa, gray-blue color of the skin and mucous membranes due to methæmoglobinæmia, jaundice, methæmoglobinuria, oliguria, coma, convulsions, cardiac failure.	Gastric lavage, colonic irrigation, diuretics, saline infusion, pilocarpine (subcutaneous stimulants). (Avoid acids and carbonated fluids.)
Bromine Bromine vapor	Stimulation of the respiratory mucous membrane, cough, asphyxia, delirium, headache, yellow color of the mucous membranes, vomiting, diarrhœa, coma.	Fresh air, inhalations of steam or of ½% carbolic acid solution.
Iodine Iodine solution and Iodides	Burning in the mouth and pharynx, coryza, dyspnœa (œdema of larynx), nausea, abdominal pain, vomiting, headache, dizziness, hæmoglobinuria or anuria, acne.	Gastric lavage, albumin and sodium hyposulphite by mouth, opiates, when necessary tracheotomy.
Inorganic acids (a) sulphuric acid	Corrosion of the buccal, pharyngeal, œsophageal and gastric mucous membrane with white and later black membranes, vomiting, small pulse, subnormal temperature, delirium, albumin and blood in the urine.	Gastric lavage with soap, albumin, oil and later water, milk, magnesia, stimulants, salycilates by mouth and as a gargle.
(b) hydrochloric acid	Corrosion of the mouth and pharynx; membranes white similar to diphtheria, vomiting, sometimes hæmatemesis, albuminuria, hæmaturia.	Gastric lavage, protein, milk, water, magnesia.

INORGANIC POISONS—*Continued*

Poison	Symptoms	Therapy
Inorganic acids—(*Continued*) (c) nitric acid	Corrosion of the mouth and pharynx; membrane yellowish, vomiting, swelling of the tongue, anuria, constipation.	As in HCl poisoning.
Acetic acid	Corrosion of the mouth, pharynx, larynx and upper portion of the œsophagus; membrane pure white, vomiting.	Milk, water, magnesia, gastric lavage.
Ammonia	Corrosion of the mucous membranes; white membrane, pain in the mouth, vomiting, ptyalism, dyspnœa, convulsions, dizziness, paralyses.	Weak organic acids (dilute acetic or citric acid), albumin, milk, oil, when necessary tracheotomy.
Phosphorus	Vomiting; vomitus phosphorescent in the dark; pain in the abdomen, diarrhœa, hæmorrhage from the nose, uterus and into the skin, albuminuria; after several days jaundice and the appearance of acute yellow atrophy ot the liver.	Gastric lavage with potassium permanganate or hydrogen peroxide (1–3%); emetics, saline infusion. Avoid all fats and milk.
Arsenic and Arsenic preparations	Cholera-like diarrhœa, dizziness, headache, collapse, convulsions, optic atrophy; with chronic poisoning polyneuritis with paralyses.	Emetics (tartar emetic), gastric lavage, antidotes of arsenic, magnesia, milk, lime water, purgatives.
Caustic potash and sodium hydrate	First degree corrosion, penetrating corrosion, deliquescent membrane, vomiting.	Vegetable acids (vinegar, citric acid), ice, ice water, mucoid preparations, cocaine for local anæsthesia, opiates.
Silver nitrate	Corrosion of the mouth; white membrane; vomiting of caseous masses of AgCl, pain in the abdomen; chronic poisoning: argyria (grayish discoloration of the skin).	Gastric lavage, common salt (not too much), albumin, milk, ice.
Copper Verdigris and copper-sulphate	Local corrosion, metallic taste, vomiting of green material, colic, bloody diarrhœa, tenesmus, jaundice, dizziness, convulsions, paralyses.	Plenty of warm water by mouth. Emetic, gastric lavage, magnesia, milk, animal charcoal, reduced iron.
Lead compounds (red-lead, white-lead, lead acetate, lead chromate)	Slight corrosion of œsophagus. Vomiting of grayish-white material, salivation, stomatitis, dark discoloration of the gums, intense pain in the abdomen, bloody stools, later obstruction. In chronic lead poisoning: blue line on gums, gout, nephritis, paralyses (e.g., paralysis of radial nerve), hard, slow pulse, stippled red blood cells.	Emetic, gastric lavage, purgative, sodium- and magnesium-sulphate, albumin, milk; later opium and potassium iodide.
Mercury (a) corrosive preparations (sublimate, mercuric iodide)	Corrosion of mucous membrane of mouth, definite metallic taste, bloody vomitus, bloody stools, colitis, salivation, stomatitis, anuria, albuminuria, collapse, chronic poisoning: Tremor.	Gastric and intestinal lavage, milk or solution of albumin, wood charcoal, ferrum pulveratum, magnesia.
(b) Weak preparations (calomel and mercurous iodide)	Stomatitis, gastric distress, diarrhœa.	Water by mouth, promotion of diuresis.
Chromic acid compounds	Corrosion of the upper air passages; membrane yellowish-red, vomiting, diarrhœa, nephritis with hæmaturia, dyspnœa, coma, convulsions.	Gastric lavage, sodium bicarbonate, magnesium carbonate and lead acetate.

INORGANIC POISONS—*Continued*

Poison	Symptoms	Therapy
Hydrogen sulphide, sewer gas	Irritation of the conjunctiva and upper air passages, headache, dizziness, nausea, diarrhœa, convulsions, coma.	Fresh air, artificial respiration, stimulants. Prophylaxis: sewers should be partly filled with sulphate of iron.

ALIPHATIC HYDROCARBONS

Benzine	Headache, dizziness, collapse (autopsy: hæmorrhage into the lung parenchyma).	Fresh air, artificial respiration, gastric lavage.
Methane; Petroleum	Intoxication, dizziness, cyanosis, heart failure, convulsions, vomiting, pain in the stomach, oliguria.	Fresh air, artificial respiration. If petroleum has been swallowed: gastric lavage, emetics and purgatives.
Carbon disulphide	Narcosis with pallor of the face, lips blue, pupils dilated, temperature subnormal, odor of radishes on the breath, dizziness and headache.	Fresh air, artificial respiration, stimulants.
Alcohol	Drunkenness, loss of consciousness, widely dilated pupils, slow respirations, small, rapid pulse, fall in temperature, sometimes ataxia.	Gastric lavage, artificial respiration, camphor, caffeine.
Methyl alcohol	Vomiting, pain in the abdomen, paralyses, disturbance of vision, amaurosis, collapse, difficult respiration.	Gastric lavage, diuretics, force fluids, strong coffee, stimulants.
Chloroform	Narcosis, cardiac failure.	Artificial respiration.
Bromoform	Drunkenness, narcosis, cyanosis, myosis, disturbances of respiration, rapid irregular pulse, collapse.	Gastric lavage, camphor, artificial respiration.
Iodoform	Sleeplessness, vomiting, heart failure, dizziness, anxiety, hallucinations, confusion, excitement, collapse.	Stimulation of diuresis, subcutaneous saline infusion, bromides.
Sulphonal	Drowsiness, with subacute or chronic intoxication, obstinate constipation, porphyrinuria.	Colonic irrigation with warm water, artificial respiration, caffeine.
Veronal (Barbituric acid compounds) Barbital, and luminal	Drowsiness, delirium, dizziness, jactitation. Vomiting, extremities cold, pupils fixed, cyanosis, porphyrinuria.	Gastric lavage with 0.5% tannin solution, caffeine, strong black coffee, artificial respiration.
Chloral hydrate	Drowsiness, delirium, cyanosis, slow stertorous respiration, coma, bradycardia and hypothermia.	Gastric lavage, artificial respiration, strychnine, caffeine, warmth to the skin.
Oxalic acid	Corrosion of the upper air passages, (white membrane), dysphagia, vomiting, collapse, cyanosis, mydriasis, slow and difficult respiration, heavy albuminuria, anuria, somnolence, convulsions.	Gastric lavage, calcium preparations, magnesium sulphate, milk, albumin, opiates, stimulants.
Cyanides (HCN & KCN)	Asphyxia, dyspnœa, mydriasis, cyanosis, clonic-tonic convulsions, generalized paralysis, breath smells of prussic acid.	Emetics, (apomorphine), gastric lavage, with potassium permanganate, artificial respiration, stimulants, atropine subcutaneously.

ALIPHATIC HYDROCARBONS—*Continued*

Poison	Symptoms	Therapy
Nitroglycerine	Tachycardia, redness of the face, headache, roaring in the ears, photophobia, nausea, vomiting, abdominal pain, paralysis, dyspnœa, collapse, hæmaturia and glycosuria.	Gastric lavage, stimulants particularly camphor, artificial respiration.

AROMATIC HYDROCARBONS

Nitrobenzol	Blue-gray discoloration of the face, and exposed parts due to methæmoglobinæmia, bitter-almond odor of the breath, headache, exhaustion, vomiting, coma, first with myosis, later with mydriasis, pulse small and irregular, convulsions, trismus.	Gastric and colonic lavage, purgatives, (no oil), transfusions, venesection, artificial respiration, stimulants (no alcohol).
Anilin, antipyrene, phenacetin	Hypothermia, methæmoglobinæmia, dyspnœa, palpitations, headache, convulsions, brownish-black urine.	Fresh air, oxygen inhalations, gastric lavage, saline purgatives, camphor.
Carbolic acid and Lysol	Corrosion of the mouth, pharynx and œsophagus, odor of phenol, convulsions, coma, cardiac failure, myosis, loss of corneal and patellar reflexes; urine dark green, lævo-rotation of polarized light due to glycuronic acid, increase in urinary sulphates.	Gastric lavage, soap-suds by mouth, sodium sulphate, transfusion, artificial respiration.

VEGETABLE POISONS

Mushrooms (a) mild forms (Russula emetica, Boletus satanas)	Acute gastro-enteritis. After some forms the red pigment of the mushroom appears in the urine where it produces, with Heller's test, a reddish brown discoloration of the phosphates which are precipitated.	
(b) Moderately severe forms (Agaricus, phalloides)	Vomiting and diarrhœa with collapse, delirium or coma.	Gastric lavage, fluid per rectum, atropine, caffeine, tannin, stimulants, ice bag to the head, transfusion, oxygen inhalation.
(c) Severe forms (Agaricus muscarious and Pantherinus)	Maniacal excitement with convulsive muscular contractions or coma, or alternating periods of excitement and depression.	
(d) Most severe forms (Agaricus crustuliniformis)	Ptyalism, hyperperistalsis, narrowing of the pupils and collapse (muscarinism).	
(e) Morchella esculenta	Vomiting, diarrhœa, jaundice, hæmoglobinuria, dizziness, mental confusion, coma.	Gastric lavage, emetics, venesection.
Male-fern extract	Gastro-enteritis, dizziness, tremors, dyspnœa, stupor, myosis, shrinking of the visual field, amaurosis.	Gastric and colonic lavage, cracked ice by mouth, opium.
Colchicin	Gastro-enteritis, diarrhœa, collapse, tremor, twitchings of the face and extremities, generalized tonic and clonic convulsions, stupor, delirium.	Gastric and colonic lavage, purgatives, tannic acid, opium, force fluids, saline infusion.

VEGETABLE POISONS—*Continued*

Poison	Symptoms	Therapy
Cannabis indica (Indian hemp)	Acute psychosis with hallucinations, illusions, delirium, dry mouth, tachycardia, cardiac irregularity, mydriasis.	Gastric lavage, emetics, warm bath, chloral hydrate.
Coniin (hemlock)	Paralysis beginning in the legs, extending upwards to the arms and finally involving the musculature of respiration, epileptiform convulsions, hypothermia, bradycardia, cyanosis, mydriasis.	Gastric lavage, emetics, artificial respiration, stimulants, diuretics.
Digitalis (foxglove)	Nausea, vomiting, diarrhœa, dyspnœa, irregular pulse, (pulsus bigeminus) visual disturbances, coma.	**Atropine,** caffeine, nitroglycerine.
Tropeins (atropine, hyoscyamin, scopolamin, belladonna)	Dry mouth and pharynx, thirst, dysphagia, tachycardia, palpitations, redness of the face, mydriasis, ataxia, excitement, delirium, clonic convulsions.	Gastric and colonic lavage, physostigmin, morphine.
Strychnine	Muscle pain, spasticity and cramps in the muscles, strabismus, tetanus, opisthotonus, hyper-active reflexes, exophthalmos, cyanosis, dyspnœa, suffocation.	Gastric lavage with tannate apomorphine, chloral hydrate, chloroform anæsthesia, bromides, paraldehyde, absolute rest, artificial respiration.
Curare	Generalized muscular paralysis, including the muscles of respiration, due to paralysis of the motor endings, death from asphyxia.	Artificial respiration, stimulants, caffeine, alcohol.
Santonin	Yellow vision (xanthopsia), nausea, headache, dizziness, ptyalism, staggering gait, muscular twitchings, somnolence.	Gastric and colonic lavage, purgatives, (calomel) chloral hydrate, stimulants.
Morphine	Somnolence, dysuria, nausea, vomiting, myosis, depression of respiration, bradycardia, coma.	Gastric lavage, heat to the skin, tannic acid, potassium iodide, atropine, potassium permanganate, caffeine, artificial respiration. (**Inhalation of CO_2 and oxygen.**—ED.)
Cocaine	Dry mouth and pharnyx, dysphagia, collapse, small rapid pulse, tachycardia, cold sweats, polyuria, lassitude, hallucinations, delirium, muscular twitchings, convulsions, mydriasis, pallor of the face and mucous membranes.	Inhalation of amyl nitrite, artificial respiration, cold sponge.
	With the use of cocaine for **lumbar puncture,** nausea, vomiting, headache, chill, depression of respiration, sleeplessness, paræsthesiæ in the extremities, tachycardia collapse, coma.	Prophylaxis: The addition of adrenalin to the cocaine solution.
Ergot	Anorexia, nausea, dry mouth, vomiting, colic, pallor of the skin, formication, small hard pulse, muscular weakness, dizziness, mydriasis, delirium, coma.	Gastric lavage, emetics, purgatives, salol, stimulants, amyl nitrite.
	Chronic poisoning: Pain and coldness of the hands and feet, gangrene.	Local heat to relieve vascular spasm.

VEGETABLE POISONS—*Continued*

Poison	Symptoms	Therapy
Nicotine	Ptyalism, dizziness, vomiting, cold sweats, diarrhœa, small irregular pulse, myosis, visual disturbances, convulsions. Chronic abuse of this drug: Cardiac irregularity, arteriosclerosis, gastric and intestinal disturbances.	Caffeine, tannin, gastric lavage, opiates, atropine.
ANIMAL POISONS		
Snake venom	Local inflammatory œdema with cyanotic discoloration and hæmorrhage, sensory disturbances. Generalized symptoms: Tremor, visual disturbances, dyspnœa, vomiting, diarrhœa, hæmorrhagic diatheses, jaundice, convulsions, paralyses, delirium, collapse.	Local: Ligature, aspiration of the wound by cupping, scarification, cauterization, injection of 3% potassium permanganate. General: Large doses of alcohol to intoxication, stimulants, and injection of immune serum.
POISON GAS		
Phosgene	Severe dyspnœa, asphyxia, diffuse bronchitis, hæmoptysis, pulmonary œdema, exhaustion, cyanosis, pain in the chest, loss of tendon reflexes, nephritis.	Rest in bed, force fluids, oxygen inhalation, venesection, hot compresses, stimulants, saline infusion.

MAXIMAL DOSES OF DRUGS

	Maximum single dose		Maximum daily dosage	
	Grams	Grains	Grams	Grains
Acetanilidum	0.5	7 1/2	1.5	22 1/2
Acidum arsenicosum	0.005	1/2	0.015	1/4
Acidum diæthylbarbituricum	0.75	12	1.5	22 1/2
Æthylmorphinum hydrochloricum	0.1	1 1/2	0.3	5
Agaricinum	0.1	1 1/2	....	....
Amylenum hydratum	4.0	60	8.	120
Amylium nitrosum	0.2	3	0.5	7 1/2
Apomorphinum hydrochloricum	0.02	1/3	0.06	1
Aqua amygdalarum amararum	2.	30	6.	90
Argentum nitricum	0.03	1/2	0.1	1 1/2
Arsacetin	0.2	3	....	....
Aspidinolfilicin. oleo solut.	20.	300	20.	300
Atropinum sulfuric.	0.001	1/60	0.003	1/20
Bromoformium	0.5	7 1/2	1.5	22 1/2
Cantharides	0.05	3/4	0.15	2 1/4
Chloral. formamidat.	4.	60	8.	120
Chloralum hydratum	3.	45	6.	90
Chloroformium	0.5	7 1/2	1.5	22 1/2
Cocain. hydrochloric.	0.05	3/4	0.15	2 1/4
Cocain. nitric.	0.05	3/4	0.15	2 1/4
Codeinum phosphor.	0.1	1 1/2	0.3	4 1/2
Colchicin	0.002	1/30	0.005	1/12
Creosotum	0.5	7 1/2	1.5	22 1/2
Diacetylmorphinum hydrochloricum	0.005	1/12	0.015	1/4
Dihydrooxycodeinon.hydrochloricum	0.03	1/2	0.1	1 1/2
Dionin	0.1	1 1/2	0.3	4 1/2
Emetin. hydrochloricum	0.05	3/4	0.1	1 1/2
Eukodal	0.03	1/2	0.1	1 1/2
Extract. Belladonnæ	0.05	3/4	0.15	2 1/4
Extract. Colocynthidis	0.05	3/4	0.15	2 1/4
Extract. Filicis	10.	150	10.	150
Extract. Hyoscyami	0.15	2 1/4	0.5	7 1/2
Extract. Opii	0.075	1	0.25	4 3/4
Extract. Strychni	0.05	3/4	0.1	1 1/2
Filmaronol	20.	300	20.	300
Folia Belladonnæ	0.2	3	0.6	9
Folia Digitalis	0.2	3	1.	15
Folia Hyoscyami	0.4	6	1.2	18
Folia Stramonii	0.2	3	0.6	9
Fructus Colocynthidis	0.3	4 1/2	1.0	15
Glandulæ Thyreoideæ siccat.	0.5	7 1/2	1.0	15

MAXIMAL DOSES OF DRUGS—*Continued*

	Maximum single dose		Maximum daily dosage	
	Grams	Grains	Grams	Grains
Gutti	0.3	$4^1/_2$	1.0	15
Herba Lobeliæ	0.1	$1^1/_2$	0.3	$4^1/_2$
Heroin. hydrochloric.	0.005	$^1/_{12}$	0.015	$2^1/_4$
Homatropinum hydrobromicum	0.001	$^1/_{60}$	0.003	$^1/_{20}$
Hydrargyr. bichlorat.	0.02	$^1/_3$	0.06	1
Hydrargyr. biiodatum	0.02	$^1/_3$	0.06	1
Hydrargyr. chlorat. by injection	0.1	$1^1/_2$	....	....
Hydrargyr. cyanatum	0.01	$^1/_6$	0.03	$^1/_2$
Hydrargyr. oxycyanat.	0.01	$^1/_6$	0.03	$^1/_2$
Hydrargyr. oxydatum	0.02	$^1/_3$	0.06	1
Hydrargyr. oxydatum via humida paratum	0.02	$^1/_3$	0.06	1
Hydrargyr. salicylic.	0.15	$2^1/_4$	....	....
Hydrastininium chlorat.	0.05	$^3/_4$	0.15	$2^1/_4$
Liquor Kaliiarsenicosi	0.5	$7^1/_2$	1.5	$22^1/_2$
Lobelin. hydrochloricum	0.02	$^1/_3$	0.1	$1^1/_2$
Luminal	0.4	6	0.8	12
Luminal-Natrium	0.4	6	0.8	12
Medinal	0.75	11	1.5	$22^1/_2$
Methylsulfonalum	1.0	15	2.0	30
Morphinum hydrochl.	0.03	$^1/_2$	0.1	$1^1/_2$
Narcophin	0.03	$^1/_2$	0.1	$1^1/_2$
Natrium acetylarsanilicum	0.2	3	....	....
Natrium nitrosum	0.3	$4^1/_2$	1.0	15
Natr. phenylæthylbarbituricum	0.4	6	0.8	12
Nitroglycerin. solut.	0.1	$1^1/_2$	0.4	6
Ol. Chenopodii anthelminthici	0.5	$7^1/_2$	1.0	15
Oleum crotonis	0.05	$^3/_4$	0.15	$2^1/_4$
Opium pulveratum	0.15	$2^1/_4$	0.5	$7^1/_2$
Opium concentrat.	0.03	$^1/_2$	0.1	$1^1/_2$
Papaverin. hydrochloricum	0.2	3	0.6	9
Paraldehydum	5.0	75	10.0	150
Phosphorus	0.001	$^1/_{60}$	0.003	$^1/_{20}$
Phosphor. solut.	0.2	3	0.6	9
Physostigmin. salicyl.	0.001	$^1/_{60}$	0.003	$^1/_{20}$
Physostigmin. sulfuric.	0.001	$^1/_{60}$	0.003	$^1/_{20}$
Pilocarpin. hydrochl.	0.02	$^1/_3$	0.04	$^2/_3$
Pilulæ asiatic	5. pills	....	15. pills	....
Plumbum aceticum	0.1	$1^1/_2$	0.3	$4^1/_2$
Podophyllinum	0.1	$1^1/_2$	0.3	$4^1/_2$
Pulvis Ipecacuanhæ opiatus	1.5	$22^1/_2$	5.	75
Santoninum	0.1	$1^1/_2$	0.3	$4^1/_2$
Scopolaminumhydrobromicum	0.001	$^1/_{60}$	0.003	$^1/_{20}$
Semen Strychni	0.1	$1^1/_2$	0.2	3

MAXIMAL DOSES OF DRUGS—*Continued*

	Maximum single dose		Maximum daily dosage	
	Grams	Grains	Grams	Grains
Strophanthin	0.001	$1/60$	0.003	$1/20$
Strychninum nitric.	0.005	$1/12$	0.01	$1/5$
Sulfonalum	1.0	15	2.0	30
Suprarenin. hydrochl.	0.001	$1/60$	....	....
Tartarus stibiatus	0.1	$1\,1/2$	0.3	$4\,1/2$
Theophyllinum	0.5	$7\,1/2$	1.5	$22\,1/2$
Tinct. Cantharidum	0.5	$7\,1/2$	1.5	$22\,1/2$
Tinct. Colchici	2.0	30	6.0	90
Tinct. Colocynthidis	1.0	15	3.0	45
Tinct. Digitalis	1.5	$22\,1/2$	5.0	75
Tinct. Iodi	0.2	3	0.6	9
Tinct. Lobeliæ	1.0	15	3.0	45
Tinct. Opii crocata	1.5	$22\,1/2$	5.0	75
Tinct. Opii simplex	1.5	$22\,1/2$	5.0	75
Tinct. Strophanthi	0.5	$7\,1/2$	1.5	$22\,1/2$
Tinct. Strychni	1.0	15	2.0	30
Trionalum	1.0	15	2.0	30
Veratrinum	0.002	$1/30$	0.005	$1/12$
Veronalum	0.75	11	1.5	$22\,1/2$
Veronal-Natrium	0.75	11	1.5	$22\,1/2$
Yohimbin. hydrochloricum	0.03	$1/2$	0.1	$1\,1/2$

SOLUBILITY OF SOME USEFUL DRUGS

	Water	Alcohol	Ether
Acid arsenicos.	55	—	—
" boric.	22	25	—
" carbolic (phenol)	15	m.s	m.s
" salicylic.	500	m.s	v.s
" tannic.	1	2	—
Adalin.	sl.s	m.s	—
Anæsthesin.	sl.s	m.s	m.s
Antipyrin (Phenyldimethylic. Pyrazolon)	1	1	80
Apomorphin. hydrochlor.	50	40	—
Argent. nitric.	0.5	14	—
Arsacetin.	10	—	—
Aspirin (acid. acetylsalicyl.)	300	m.s	20
Atophan	—	in Alkal.	sl.s
Atropin. sulphuric	1	3	s
Borax	25	—	—
Bromural	sl.s	s	s
Calcium chlorat.	v.s	v.s	—
Calcium lactic	20	—	—
Chinin. hydrochloric	32	3	—
Chloralhydrat	m.s	m.s	m.s
Chloroform	sl.s	m.s	m.s
Cocain. hydrochloric	0.75	m.s	—
Codein. phosphoric	4	s	—
Coffein. sod.-salicyl.	2	50	—
Coffein. pur.	80	50	600
Collargol.	s	—	—
Cycloform.	sl.s	m.s	m.s
Dionin.	12	s	—
Eukodal	6	60	—
Extr. Filicis	—	sl.s	s
Extr. spissa varia	Cloudy s.	Cloudy	—
Guaiacol. carbonic	—	heat s	sl.s
Heroin. hydrochloric	m.s	sl.s	
Hexamethylentetramin (Urotropin)	1.5	10	—
Homatropin. hydrobromic.	4	18	—
Hydrargyr. bichlorat.	16	3	17
" iodide	—	250	60
" cyanat.	12	12	sl.s
" oxycyanat.	19	—	—
" salicylic.	—	—	—
Iodoform	—	70	10
Iodum	4000	9	m.s

	Water	Alcohol	Ether
Pot. chloric.	15	130	—
Pot. iodide	0.75	12	—
Coagulen.	10	—	—
Creosot.	sl.s	s	s
Creosot. carbonic	—	s	s
Luminal.	1100	10	15
Luminal. sodium.	1.2	sl.s	—
Menthol.	v.sl.s	m.s	m.s
Medinal.	4	sl.s	—
Melubrin	m.s	sl.s	—
Migrænin	m.s	m.s	—
Morphium hydrochl.—Naphthol	v.sl.s	m.s	m.s
Narcophin	12	25	—
Sod. kakodylic	m.s	—	—
Sod. salicylic	1	6	—
Novocain.	1	8	—
Orthoform	sl.s	6	50
Papaverin. hydrochl.	40	sl.s	—
Paraldehyd.	10	m.s	m.s
Phenacetin.	1400	16	—
Phosphorus	—	sl.s	80
Physostigmin. salicyl	85	12	—
Pilocarpin. hydrochl.	m.s	m.s	—
Plumb. acetic.	2.3	29	—
Protargol.	m.s	—	—
Pyramidon	20	v.s	s
Resorcin.	1	1	m.s
Sacchar. amylac. (Grape sugar)	1.5	—	—
Salipyrin.	250	m.s	s
Salol	v.sl.s	10	0.3
Salvars. sod. or Neo-Salvarsan.	m.s	—	—
Santonin.	v.sl.s	44	75
Scopolamin hydrobr.	m.s	m.s	v.sl.s
Strophanthin.	100	sl.s	sl.s
Strychnin. nitric.	90	70	—
Tartar. stibiat.	17	—	—
Theobromin. Sod. salicyl. (Diuretin)	1	—	—
Theocin. (Theophyll)	sl.s	sl.s	—
Thymol.	1100	m.s	m.s
Trigemin.	65	2	10
Trional.	450	m.s	m.s
Veronal	170	m.s	m.s

Explanation of Abbreviations: s = soluble; m.s = moderately soluble; v.s = very soluble; sl.s = slightly soluble; v.sl.s = very slightly soluble.

TABLE OF APPROXIMATE EQUIVALENTS

1	gr.	equals	64	mgm.
1/2	gr.	"	32	mgm.
1/4	gr.	"	16	mgm.
1/8	gr.	"	8	mgm.
1/10	gr.	"	6	mgm.
1/16	gr.	"	4	mgm.
1/32	gr.	"	2	mgm.
1/40	gr.	"	1.5	mgm.
1/50	gr.	"	1.2	mgm.
1/60	gr.	"	1.	mgm.
1/75	gr.	"	0.8	mgm.
1/100	gr.	"	0.6	mgm.
1/150	gr.	"	0.4	mgm.
1/200	gr.	"	0.3	mgm.

1.5	gr.	equals	0.1	gm.
2.	gr.	"	0.13	gm.
2.5	gr.	"	0.16	gm.
3.	gr.	"	0.2	gm.
4.	gr.	"	0.25	gm.
5.	gr.	"	0.3	gm.
10.	gr.	"	0.6	gm.
15.	gr.	"	1.	gm.
20.	gr.	"	1.3	gm.
25.	gr.	"	1.6	gm.
30.	gr.	"	2.	gm.

INDEX